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RHEUMATIC INFECTIONS OCCURRING IN THE FIRST THREE YEARS OF LIFE

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NEW YORK

Coburn [1] called attention to the changes occurring from one year to another in the clinical manifestations of the rheumatic state. More striking, even, are the modifications through which the clinical concept of the rheumatic state has passed in recent years; and it has seemed to us of some interest to review the records of our youngest group of rheumatic patients, in the hope of obtaining a picture of the clinical and anatomic manifestations of the disease at an early age. We had the impression that rheumatic fever expresses itself in a subject under 3 years of age in a manner different from that by which one is accustomed to recognize it in older children. At the same time, its infrequency in early life throws a formidable obstacle in the path of the individual observer who attempts to formulate from his own experience a not too one-sided picture of the disease. We have selected from the records of the Babies Hospital, covering a period of about twenty-five years, a group of 24 cases, in all of which the disease appears to have begun before the age of 3 years and in which the evidence warrants, in our judgment, the diagnosis of rheumatic infection.

Rheumatic infection is predominantly a disease of childhood. Analysis of the records of large groups of cases has brought out the fact that the greatest number of first attacks occurs in children between the ages of 5 and 15 years. Poynton [2] found the average age of onset to be 7 years; Coombs,[3] 10.2 years; Wilson, Lingg and Croxford,[4]

From the Babies Hospital and Department of Diseases of Children, Columbia University College of Physicians and Surgeons.

Part of the material contained in this paper was presented before the American Pediatric Society at the meeting in Washington, D. C., May 8, 1933.

1. Coburn, A. F.: The Factor of Infection in the Rheumatic State, Baltimore, Williams & Wilkins Company, 1931.

2. Poynton, F. J.: The Nature and Symptoms of Cardiac Infection in Childhood: II. Rheumatic Heart Disease, Brit. M. J. **1**:417 (April 13) 1918.

3. Coombs, C. F.: Rheumatic Heart Disease, New York, William Wood & Company, 1924.

4. Wilson, M. G.; Lingg, C., and Croxford, G.: Statistical Studies Bearing on Problems in the Classification of Heart Disease: III. Heart Disease in Children, Am. Heart J. **4**:164 (Dec.) 1928.

7.3 years, and Mackie,[5] including patients of all ages and dividing them into groups in five year age periods, found the greatest incidence to be between 10 and 15 years.

These series and others illustrate that rheumatic infection is rare, although not exceptional, before the age of 3 years. Still,[6] in 1,027 cases of rheumatic infection in children, saw no patients under the age of 2 years and only 8 under the age of 3 years. Findlay,[7] in 364 cases of rheumatic arthritis, found none occurring before the age of 2 years and 4 during the third year of life; and among 457 patients with rheumatic cardiac disease there were 2 aged between 1 and 2 years and 3 between 2 and 3 years. Smith and Sutton,[8] in 623 cases, reported 3 patients between 1 and 2 years and 7 between 2 and 3 years of age. A combination of these figures shows that of 2,884 cases of rheumatic infection, 40, or 1.3 per cent, occurred in the first 3 years of life. Small groups of cases of rheumatic infection in young children have been reported by Koplik,[9] Miller,[10] Bass,[11] Schroeder,[12] Smith,[13] Denzer,[14] Poynton,[15] Rothman and Leonard [16] and others.

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5. Mackie, T. T.: An Analytical Study of Three Hundred and Ninety-Three Cases of Rheumatic Fever and Eighty-Nine Cases of Chorea, Am. J. M. Sc. **172**:199 (Aug.) 1926.

6. Still, G. F.: Common Disorders and Diseases of Childhood, New York, Oxford University Press, 1909.

7. Findlay, L.: The Rheumatic Infection in Childhood, New York, Longmans, Green & Co., 1931.

8. Smith, C. H., and Sutton, L. P.: Heart Disease in Infancy and Childhood, in Haynes, R. S.: Clinical Pediatrics, New York, D. Appleton & Company, 1930, vol. 18.

9. Koplik, H.: Acute Articular Rheumatism in Nursing Infants, New York M. J. **47**:673, 1888.

10. Miller, D. J. M.: Acute Articular Rheumatism in Infants Under One Year, with the Report of a Case, Arch. Pediat. **16**:686, 1899.

11. Bass, M. H.: The Cutaneous Manifestations of Acute Rheumatic Fever in Childhood, M. Clin. North America **2**:201 (July) 1918.

12. Schroeder, L. C.: Observations on the Etiology and Pathology of Chorea Minor, J. A. M. A. **79**:181 (July 15) 1922.

13. Smith, A. deG.: Rheumatism and Its Manifestations in Children Under Five Years, Arch. Pediat. **39**:799, 1922.

14. Denzer, B. S.: Rheumatic Heart Disease in Children Under Two Years of Age: Report of Three Cases, J. A. M. A. **82**:1243 (April 19) 1924.

15. Poynton, F. J.: A Contribution to the Study of Rheumatism Based upon a Study of Fifty-Two Cases in Children Under Five Years of Age, and an Analysis of One Hundred Cases of Fatal Suppurative Pericarditis in Childhood, Quart. J. Med. **1**:225 (April) 1908.

16. Rothman, P. E., and Leonard, B. W.: Cardiac Failure in Children Under Five Years of Age, with Special Reference to Acute Rheumatic Myocarditis, Am. J. Dis. Child. **35**:1 (Jan.) 1928.

The age of onset of symptoms and the age on admission to the hospital are shown in figure 1. It is of some interest that after the age of 18 months the distribution of cases in successive half-year periods was fairly uniform—in other words, the curve of incidence did not rise noticeably. After the third birthday the number of cases increased sharply, but we have made no attempt to give a figure for comparison, because prior to 1929 the Babies Hospital admitted few patients more than 3 years old, and it is only since then that the figures on morbidity for the entire period of childhood approach a normal distribution.

The family history in rheumatic cases is generally regarded as important, partly because of the possible hereditary transmission of susceptibility in some anatomically recognizable constitutional type or otherwise, and partly because of the possibility of direct transfer of the infection from one member of the family to another. Cheadle [17]

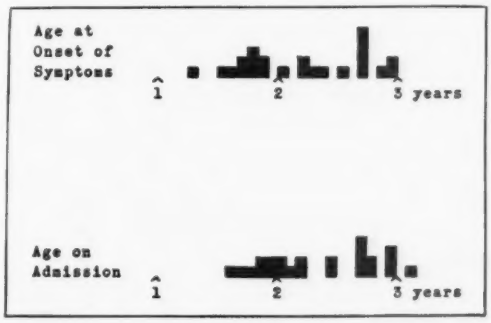

Fig. 1.—Age distribution in twenty-four cases of rheumatic infection in early life.

stated that a child in a rheumatic family has five times as great a chance of having the disease as does a child in a healthy family. Paul and Salinger,[18] in approaching the study of the epidemiology of rheumatic infection, studied the spread of the disease through families. Their results indicate the frequency with which the disease appears in one member of a family simultaneously with or immediately subsequent to its appearance in another member. They found evidence of the periodic occurrence of activity of the disease involving the family. In no instance in our series was there a history of simultaneous acute rheumatic fever in the home, and it is our impression that the frequency with which past rheumatic infection in one or the other parent occurred was no greater than one would expect to find in any family.

17. Cheadle, W. B.: The Various Manifestations of the Rheumatic State as Exemplified in Childhood and Early Life, London, Smith, Elder & Company, 1889.

18. Paul, J. R., and Salinger, R.: The Spread of Rheumatic Fever Through Families, J. Clin. Investigation **10**:33 (April) 1931.

On the whole, the history of our patients was likewise not abnormal, revealing what we have taken to be only an average incidence of infections of the respiratory tract. Scarlet fever preceded the onset of rheumatic symptoms by an interval of two weeks in one case; in another, it followed the onset by one month. The frequency with which an infection of the upper respiratory tract caused by a hemolytic streptococcus precedes the outbreak of rheumatic symptoms by an interval of from one to three weeks has only recently been established. In our series there was a history of infection of the upper respiratory tract within three weeks of the onset of rheumatic symptoms in 10 cases (42 per cent). It is possible that in the cases represented by the older records this sequence of events was not as diligently inquired

TABLE 1.—*Symptoms of Rheumatic Infection in Twenty-Four Cases Occurring in Early Life*

Symptom	Number of Patients	Proportion in the Series, per Cent
Fever	18	75
Painful and swollen joints	11	46
Heavy or rapid breathing	10	42
Loss of appetite	6	25
Vomiting	6	25
Weakness	6	25
Edema	5	21
Cough	5	21
Pallor	4	17
Irritability	3	13
Abdominal pain	2	8
Eruption	2	8
Sweating	2	8
Loss of weight	1	4
Rapid heart action	1	4
Blood in urine	1	4

into as is now the case. No bacteriologic studies of the precursor infections were made in our series.

The symptoms of the rheumatic infection, as given in the history of the present illness, are shown in table 1. While fever is seen to be the most common symptom detected by the parents, occurring in 75 per cent of the cases, its absence, or rather its inconspicuousness, in the remaining 25 per cent is perhaps of even more interest. Symptoms referable to involvement of either the joints or the heart were considered to be definitely rheumatic and were found in 20 of the 24 patients (83 per cent). Six patients showed symptoms in the joints, 9 showed symptoms attributable to cardiac failure and 5 had symptoms in both the joints and the heart. Of the symptoms dependent on a lesion that may be specifically rheumatic but is not necessarily so, particularly abdominal pain, an eruption, hematuria and possibly cough, there was only a scattered incidence. Four patients presented no specifically recognizable rheumatic symptoms. It should be pointed out, how-

ever, that many of the cardiac symptoms were vague and might well have been considered as signs of infection in general. It is also noteworthy that symptoms of an indefinite nature, such as fever, loss of appetite and weakness, outweighed (46 to 37 instances) those that might point to rheumatic infection in particular, even if we include in the latter group the questionably specific lesions and those indefinite symptoms which, in the light of subsequent physical examination, were related to cardiac damage.

It will be seen in table 2, which gives the incidence of abnormal physical signs found on examination, that by the time the patient reaches the

TABLE 2.—*Incidence of Abnormal Physical Signs Dependent on or Related to the Rheumatic Infection Detected in Twenty-Four Cases Occurring in Early Life*

	Number of Patients	Proportion in the Series, per Cent
Signs of cardiac involvement	22	92
Pericardial	8	33
Friction rub	3	
Positive roentgen evidence	4	
Aspiration of pericardial fluid	2	
Myocardial	19	79
Enlarged heart	17	
Enlarged liver	13	
Altered sounds or rhythm	8	
Endocardial	21	88
Systolic murmur	21	
Diastolic murmur	8	
Dyspnea	16	67
Edema	6	25
Cyanosis	5	21
Orthopnea	3	13
Pharyngitis or tonsillitis	16	67
Pallor	15	62
Restlessness	12	50
Vomiting	11	46
Involvement of the joints	9	38
Pneumonia	4	17
Otitis media	4	17
Cutaneous manifestations	3	13
Abdominal pain or tenderness	2	8

hospital, cardiac involvement definitely dominates the picture. Only 2 patients of the 24 did not present signs of cardiac involvement. One of these was a boy in whom there developed fever and fleeting pains in the joints with swelling three days before his third birthday. He had fever and periarticular swellings while in the hospital; there was leukocytosis, and a roentgenogram of an involved joint showed no change aside from swelling of the soft tissues. The symptoms responded to medication with salicylates, and he was discharged greatly improved at the end of sixteen days. Seven months later he showed no abnormality beyond enlargement of the tonsils. The other patient presented a history of swollen and painful joints, but during hospitalization involvement of the heart was not demonstrated, even though a doctor who saw him at home at one time detected a pericardial friction rub. At autopsy the myocardium contained numerous Aschoff bodies, and

the two layers of the pericardium were bound together by fibrous adhesions. In the entire series, therefore, involvement of the heart detectable either clinically or post mortem was present in all but 1 case (96 per cent). The partition of physical signs is more easily indicated in the table than described in detail. We may expose ourselves to criticism by listing more patients as showing endocardial than myocardial involvement. The excessive number listed in the "endocardial" group represents patients who had a systolic murmur believed to be organic in origin and not accompanied by cardiac enlargement or by other signs of myocardial insufficiency, on which evidence we are of course not prepared to hold rigidly to the anatomic diagnosis. One would expect to find dyspnea on exertion in all or nearly all of the 23 patients with cardiac involvement; dyspnea while at rest, however, was found in only 16. The relatively low incidence of edema and, particularly, of orthopnea, as compared with a parallel series of older subjects is not surprising, in view of the fact that among our patients the illness described represented in almost all instances the first evidence of rheumatic activity.

Signs of involvement of the joints were a little less frequently represented than were the symptoms in the joints given in the history. This is probably due as much to the fact that there were no objective changes as to the tendency to spontaneous disappearance and to subsidence under the influence of salicylate therapy, treatment which in former years was usually given indiscriminately to rheumatic patients whether they had painful joints or not. The cutaneous manifestations referred to were erythema in 2 instances and purpura in 1. Abdominal symptoms were present in 2 patients who went rapidly down hill with severe cardiac involvement, and it is more probable that this symptom was caused by stretching of the hepatic capsule than that it represented the specific peritoneal lesion of rheumatic fever. Autopsy was performed on 1 of these patients and showed no peritoneal involvement. Our series included no examples of chorea, rheumatic nodules or epistaxis.

There is little purpose in attempting to convey an idea of the behavior of the temperature or of the pulse rate in a group as heterogeneous as this. The average temperature was 100.2 F.; the average pulse rate, 136. One may perhaps point out the relative mildness of the fever and the relative acceleration of the pulse. The blood pressure ranged from 70 systolic and 28 diastolic to 122 systolic and 92 diastolic, with an average of 96 systolic and 58 diastolic, a value one would regard as normal for the ages represented.

There were wide variations in the levels of the erythrocyte count, the leukocyte count and the hemoglobin content of the blood. Such variations probably depend on the marked difference in the severity, duration and activity of the disease in individual patients. The degree

of anemia in rheumatic patients of this age probably depends much more on antecedent factors of nutrition and infection than on any specific connection with the rheumatic condition. The hemoglobin content varied from 20 to 84 per cent, with an average of 61 per cent (Sahli: normal, 17 Gm. per hundred cubic centimeters). The erythrocyte count varied from 1,900,000 to 5,200,000, with an average of 3,600,000, per cubic millimeter. The leukocytes varied from 9,200 to 46,000, with an average of 17,100, per cubic millimeter, and the polymorphonuclear leukocytes varied from 43 to 91 per cent, with an average of 72 per cent, of the total number of white blood cells. We have no data on the Schilling index in these patients.

The urinary observations revealed nothing more than one would expect with any infection, except in 1 patient, to be described later (case 5). Briefly, during life the urine of this patient gave a 4 plus reaction for albumin and showed numerous casts of all sorts, and autopsy showed extensive renal lesions—glomerular, interstitial and vascular—which were ascribed to the rheumatic process.

Blood cultures gave negative results in 6 patients. One patient with involvement of both the heart and the joints showed a positive culture (nonhemolytic streptococci) on two occasions and a negative culture on five. This single positive bacteriologic result may be considered by many to throw doubt on our right to include the patient in our series, but a critical review of the data forces us to the conclusion that we have less reason to discard the case than to include it. The experience is by no means unique.

There was no characteristic pattern of blood chemistry. The nonprotein nitrogen value was higher than 35 mg. per hundred cubic centimeters in 4 of 9 instances, but possibly this incidence is not greater than that found in nonrheumatic infections.

Roentgenograms have been useful in demonstrating enlargement of the heart and possibly also in lending support to a clinical diagnosis of pericardial effusion. They are probably of no help in differentiating rheumatic from other types of pulmonary involvement. The greatest service, that of providing an accurate objective criterion of progressive change in the size of the heart over a long period, was not manifest in our series because of the relatively short period over which any single patient was observed.

Electrocardiograms were made infrequently and only on the patients most recently studied. In one instance, in a patient whose symptoms appeared at 2 years and 2 months of age and who died at the age of 3 years, the electrocardiogram made a few days before death showed a P R interval of 0.12 second; the S T interval was elevated in leads II and III, and autopsy (case 4) showed changes in the myocardium, with hypertrophy of the ventricular muscle fibers and scattered Aschoff bodies.

In other patients the P R interval measured 0.12 second at 22 and 24 months of age, 0.15 second at 2 years and 9 months and 0.16 second at 2 years and 3 months. We know of no adequate normal standards for this age group, but it appears from extrapolation of the figures for older children collected by Lincoln and Nicolson [19] that the last two values cited are abnormally high.

Studies of the erythrocyte sedimentation rate were introduced at a relatively recent date in our clinic, and they were applied to but 1 patient in our series. On admission, this patient's blood showed sedimentation values of 95 mm. in one-half hour, and 142 mm. in one hour (Westergren technic). Twelve days later, parallel with clinical improvement, the patient's blood gave readings of 5 mm. in one-half hour and 17 mm. in one hour.

Of the entire series, 11 patients died, making a mortality of 45.8 per cent. Ten patients were discharged improved and 3 were discharged unimproved, all of the latter group being taken from the hospital against advice. Five patients are still being followed.

SUMMARY

The incidence of rheumatic infection in subjects under 3 years of age is probably greater than is generally recognized.

The history, symptoms, physical signs and laboratory data in these cases are variable, and the clinical picture is more often that of general infection than that of a specific disease entity.

The outstanding feature of rheumatic infection manifest during the first three years of life is cardiac damage. In our series, 96 per cent of the children exhibited, either clinically or pathologically, rheumatic heart disease.

REPORT OF CASES

The six cases in which autopsy was performed will be briefly presented.[20] Only the rheumatic lesions are reported.

CASE 1.—Josephine P., admitted to the hospital at 2 years and 10 months of age, had a history of cough at 2½ years of age, the attack lasting for six weeks. In the three weeks prior to admission there was exacerbation of the cough with fever. She weighed 10.1 Kg. (22 pounds and 3 ounces); temperature was normal, and the pulse rate rapid, and there were dyspnea, pallor, nausea and vomiting. The heart was enlarged, with precordial bulging causing asymmetry of the chest; the sounds were of poor quality. The liver was enlarged. No edema was present. The patient died three days after admission.

19. Lincoln, E. M., and Nicolson, G. H. B.: The Hearts of Normal Children: III. Electrocardiographic Records, Am. J. Dis. Child. **35**:1001 (June) 1928.

20. Dr. Martha Wollstein and Dr. Beryl H. Paige furnished the pathologic descriptions.

The observations at autopsy were as follows: The visceral pericardium was roughened over the auricles and great vessels; shreds of fibrin were present. There were numerous subepicardial petechiae. The endocardium was thickened and opaque in both auricles and to a less extent in the ventricles. There was considerable scarring of the mitral valve and its chordae tendineae. The left ventricle was dilated, and the myocardium was pale and somewhat flabby. No microscopic sections were made.

CASE 2.—Kevin L., admitted to the hospital at 3 years and 4 months of age, had a history of swollen and painful joints with high fever for six weeks, beginning at 20 months of age. This was followed by a prolonged subfebrile stage, during which the symptoms in the joints predominated. When the patient was a little less than 2 years of age a pericardial friction rub was heard by a physician, and salicylates were administered with some relief. The patient was confined to bed, and no dyspnea was observed, nor were there other direct signs of involvement of the heart. Following tonsillectomy at 2 years and 1 month of age, the patient had pneumonia, and active symptoms appeared in the joints. No abnormal cardiac signs were detected at this time. For a little over a year the symptoms in the joints were mild, but the patient was subject to repeated attacks of fever and he failed to thrive; his appetite was poor and there was marked sweating. He was admitted to the hospital with a second attack of pneumonia at 3 years and 4 months of age and died four days later. Aside from a pronounced variability of the pulse rate no abnormal cardiac signs were detected.

The observations at autopsy were as follows: The two layers of the pericardium were fused throughout with fibrous adhesions, preventing an accurate determination of the weight of the heart. The organ was, however, distinctly enlarged and hypertrophied. The myocardium was flabby, with pale areas of degeneration. No lesions of the valves were seen. Microscopically the pericardium was irregularly thickened, and in the deeper layers there were numerous focal lesions typical of rheumatic infection. The myocardium contained large numbers of Aschoff bodies. The lungs showed organized pleural adhesions, subpleural hemorrhages and areas of organized pneumonia; the first two of these three types of lesions may have been rheumatic in origin.

CASE 3.—Marion R. was admitted to the hospital at 20 months of age. The onset of symptoms occurred at 19½ months, with fever, a transient eruption and edema of the trunk and extremities; these lasted about ten days and were followed by swelling and tenderness of the joints, progressive weakness and pallor, cough and vomiting. On admission her temperature was 103 F., her weight was 10.5 Kg. (23 pounds and 3 ounces), and dyspnea, cyanosis, restlessness, cardiac enlargement with signs of mitral insufficiency and enlargement of the liver and spleen were present. There were no symptoms in the joints. She went rapidly down hill and died on the fourth day.

The observations at autopsy were as follows: The heart was enlarged and showed pericarditis of recent origin. The myocardium was soft. There were thickening and opacity of the auricular endocardium, and the mitral valve was studded with small, fresh vegetations. A single nodular vegetation was present on one of the papillary muscles. The subepicardial tissue was swollen and infiltrated by mononuclear and polymorphonuclear cells. Several Aschoff bodies were found in the myocardium. The auricular lesion was typical of rheumatic auriculitis. A mitral vegetation showed eosinophilic, hyaline material into which fibroblasts were growing. Rheumatic foci were found in the chordae tendineae and in a papillary muscle. Atypical pneumonia was present, which had the histologic

appearance of the pulmonary lesions sometimes found in older patients who have died of rheumatic fever; there were, however, no typical vascular lesions.

CASE 4.—Allan C., at 2 years and 2 weeks of age, had an attack of fever, pharyngitis and otitis media which was provisionally regarded as "grip." These symptoms lasted for three weeks and were followed by harsh, dry cough, dyspnea, anorexia, progressive loss of weight, pallor and a tendency to sweat at night. The patient was admitted to the hospital at 26 months of age with low grade fever, a rapid pulse, pallor, dyspnea and an enlarged heart with a systolic murmur audible over the entire precordia and a diastolic murmur heard only at the base. There was no enlargement of the liver. A blood count showed 19,400 leukocytes and 91 per cent polymorphonuclears. The P R interval measured 0.12 second; there was no other abnormality evident in the electrocardiogram. The patient was seriously ill for the first three weeks, then improved and was discharged after twelve weeks. The diastolic murmur had disappeared. Readmitted at 3 years and 2 weeks of age, he presented the clinical picture of progressive cardiac failure. He died at the age of 3 years and 3 months. His weight at the time of death was 14.75 Kg. (32 pounds and 6 ounces), and he measured 102 cm. (40 inches) in length.

The observations at autopsy were as follows: The heart weighed 178 Gm. (normal average for this age, 63 Gm.[21]). There were numerous punctate subepicardial hemorrhages. The myocardium was pale and flabby. The leaflets of the mitral valve were markedly thickened, with tiny yellowish vegetations superimposed, and there was thickening of some of the chordae tendineae. Two small verrucae were present on the aortic valve. The ventricular endocardium showed an area of thickening and roughening above the nonaortic leaflet of the mitral valve.

Microscopically, the myocardial fibers were irregularly hypertrophied. Typical Aschoff bodies, though rare, were present. The valvular vegetations were composed of hyaline eosinophilic material, into which fibroblasts were growing. Sections of the left auricle showed intense rheumatic auriculitis. The endocardium was thickened by an increase in connective tissue; in the zone adjacent to the cavity of the auricle there was an irregular deposit of fibrinoid material, in and about which were scattered large basophilic cells; in the zone occupying the middle third of the endocardium, large Aschoff nodules were found and in addition long rows of Aschoff cells surrounding wide bands of swollen collagen fibers, among which were moderate numbers of lymphocytes and a few polymorphonuclear leukocytes; the rest of the endocardium, adjacent to the muscle layer, was infiltrated by mononuclear and some polymorphonuclear cells.

CASE 5.[22]—After a mild attack of scarlet fever at 20 months of age, Richard R. was well for two weeks, when he began to show edema, hematuria and scattered purpuric lesions. The day before admission to the hospital at 21 months, he vomited, became drowsy and was prostrate. On admission the temperature was 101.4 F.; the pulse rate, 150; the blood pressure, 122 systolic and 92 diastolic, and the weight, 12.02 Kg. (26 pounds and 7 ounces). The patient was restless, dyspneic, pale and edematous. The heart, at first considered to be of normal size

21. Coppoletta, J. M., and Wolbach, S. B.: Body Length and Organ Weights of Infants and Children, Am. J. Path. **9**:55, 1933.

22. This case has been reported by Coburn, A. F.: Relationship of the Rheumatic Process to the Development of Alterations in Tissues, Am. J. Dis. Child. **45**:933 (May) 1933, case 6.

and free from murmurs, enlarged noticeably in the course of a few hours and there developed a loud systolic blow audible over the entire precordia; the hepatic border was at the iliac crest. A blood count showed 30,900 leukocytes and 91 per cent polymorphonuclears. The urine showed albumin (4 plus) and there were hematuria and cylindruria. The nonprotein nitrogen content of the blood was 118 mg. per hundred cubic centimeters. Death from cardiac failure occurred twenty-four hours after admission.

The observations at autopsy were as follows: The heart weighed 72 Gm. (normal average for this age, 57 Gm.[21]). The valves and endocardium were normal on gross inspection. Microscopically early rheumatic auriculitis was present (fig. 2). The nuclei of the infiltrating cells were markedly distorted into bizarre shapes and in some places were fragmented. They tended to be elongated in a direction perpendicular to wide bands of swollen collagen, forming

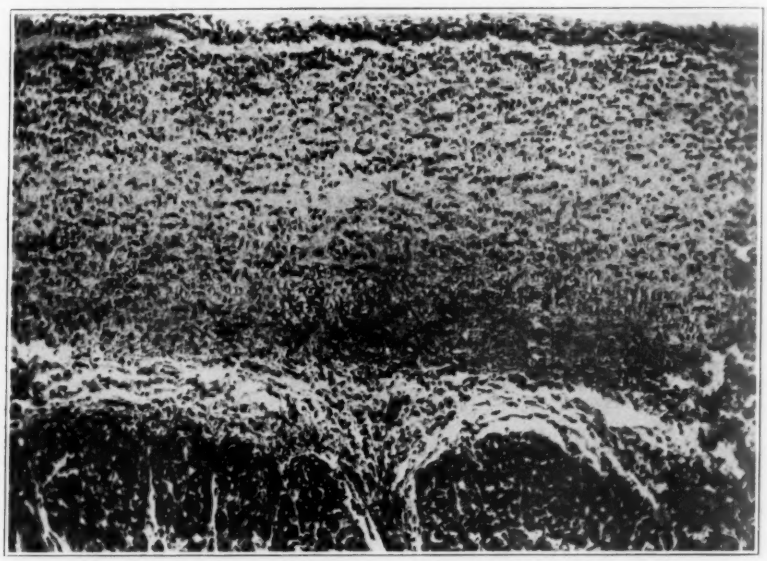

Fig. 2 (case 5).—Rheumatic auriculitis in the left auricle.

in this way a palisade arrangement. The myocardium contained collections of cells of the Aschoff type with surrounding lymphocytes (figs. 3 and 4), and in places there were polymorphonuclear leukocytes among the muscle bundles and fibers.

Many of the small arteries of the kidney showed necrosis of the walls with an infiltration of fibrin, strands of which extended beyond the muscularis to the periarterial tissue. Some of the arterial lumens were partially or completely occluded (fig. 5). Focal infiltrations of lymphocytes, polymorphonuclear leukocytes and eosinophils surrounded many of the arteries and some of the glomeruli. A few glomerular crescents were found. Some of the glomeruli were large, while others contained hyaline thrombi in their capillaries and still others showed polymorphonuclear infiltration and necrosis of the tufts. The tubules showed focal dilatation; the lumens in some areas contained red cells and in others, hyaline casts. Arterial lesions similar but of less marked degree occurred in the liver. These vascular

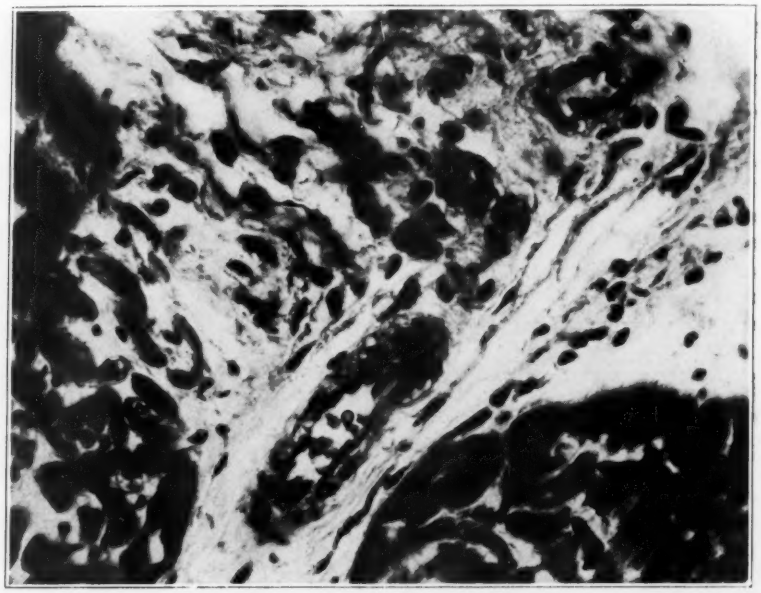

Fig. 3 (case 5).—An Aschoff body in the interstitial tissue of the myocardium.

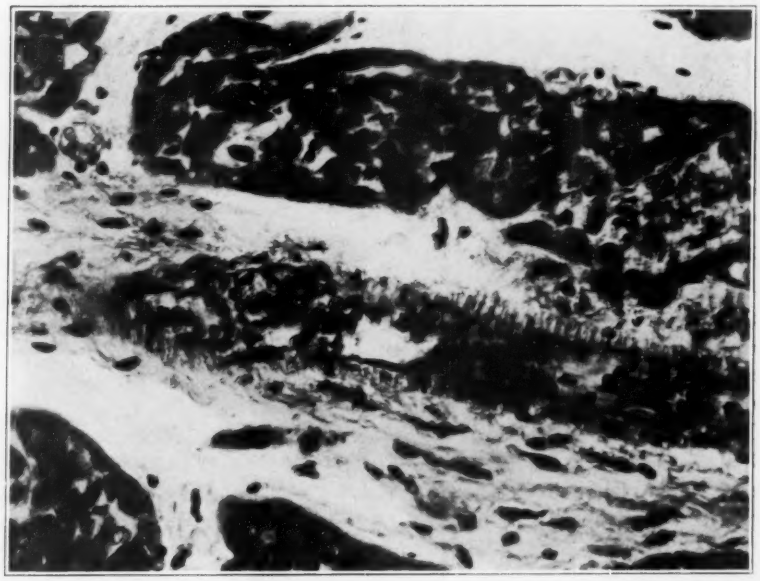

Fig. 4 (case 5).—Aschoff cells in the interstitial tissue of the myocardium.

lesions have been the subject of considerable discussion; they may represent a specific rheumatic process,[23] differing as they do from the usual renal lesion of postscarlatinal nephritis.

CASE 6.—Richard F. had poliomyelitis at 19 months of age and chickenpox at 2 years. Following bronchopneumonia at 21 months, there was a vague history of his not doing well, with two definite attacks of generalized edema, at 26 and 31 months, respectively, and enlargement of the liver. He was admitted to the hospital at 2 years and 10 months of age with fever and cough of ten days' duration, followed by dyspnea and orthopnea. He weighed 11.53 Kg. (25 pounds and 6 ounces), measured 93 cm. (36½ inches) in length and had a normal temperature and a rapid pulse rate. There was enlargement of the heart, with a soft systolic murmur audible over the entire precordia and sounds of poor quality, and the

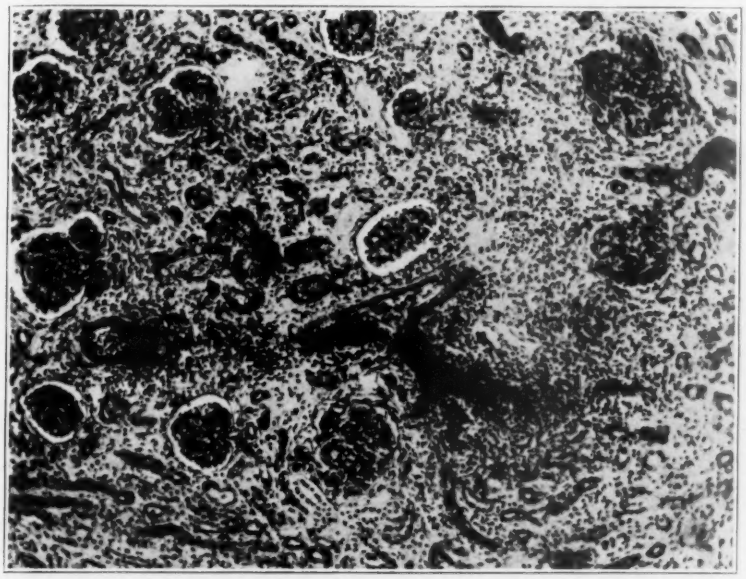

Fig. 5 (case 5).—Infiltration of fibrin into the walls of renal arterioles, with obliteration of the lumen of a branching vessel and interstitial infiltration by round cells and polymorphonuclear leukocytes. Hyaline thrombi are seen in some of the glomeruli.

liver was enlarged. There were pneumonic signs at the base of the left lung. A blood count showed 20,600 leukocytes and 85 per cent polymorphonuclears. The patient died two days after admission.

The observations at autopsy were as follows: The heart weighed 196 Gm. (normal average for this age, 60 Gm.[21]). The auricular epicardium was slightly thickened; the myocardium was pale, with dilatation of both ventricles. Both mitral leaflets were thickened, and on the nonaortic leaflet was a short row of fused verrucae. On the posterior wall of the left auricle the endocardium showed

23. Von Glahn, W. C., and Pappenheimer, A. M.: Specific Lesions of Peripheral Blood Vessels in Rheumatism, Am. J. Path. **2**:235, 1926; **3**:583, 1927.

several small yellowish plaques. Microscopically the myocardium showed many anastomosing areas of fibrosis, and there was great variation in the size of the fibers. In a few areas the interstitial tissue contained focal accumulations of lymphocytes. On the upper surface of the mitral valve was a rounded projection composed of a loose, fibrillar stroma containing scattered fibroblasts. The endocardium of the left auricle showed localized areas of thickening, in which small hillocks of cellular connective tissue projected from the endocardial surface. The auricular and valvular lesions suggested a healed rheumatic process, though the picture is unique in our experience. Two of the smaller splenic arteries showed extensive subintimal calcification. There were old infarcts in both kidneys. A blood culture made post mortem showed Haemophilus influenzae.

INJURIES TO THE VERTEBRAE AND INTERVERTEBRAL DISKS FOLLOWING LUMBAR PUNCTURE

CHARLES N. PEASE, M.D.
CHICAGO

Although it has long been known that many people complain of pain in the lower part of the back following lumbar puncture, little significance has been attached to the origin of this complaint. Investigation of this problem has recently brought to light some of the factors apparently responsible for this disability.

Introduction of the needle beyond the neural canal has been the chief agent in producing the pathologic changes to be described. Under the topic "Failure to Obtain Fluids" Levinson [1] stated: "The needle may have been introduced too far into the canal. In such cases material exuding from the intervertebral disk may clog the needle." This statement furnishes evidence that injury to the nucleus pulposus occurs, the importance of which was first emphasized by Schmorl.[2] Recent experiments by Keyes and Compere [3] led these observers to the conclusion that the loss of material from the nucleus pulposus results in pain in the back and disability, with thinning of the intervertebral disk and marginal proliferation of the adjacent vertebral bodies.

In 1924 Billington,[4] reporting on spondylitis following cerebrospinal meningitis, stated that twelve of fourteen cases he studied showed pathologic changes in the lumbar region. Because of this he conjectured the possibility that the vertebrae were affected by trauma caused by the needle and by direct inoculation with the meningococcus from the passage of the needle through the infected spinal fluid.

From the orthopedic service of Dr. Fremont A. Chandler, Children's Memorial Hospital.

Read before the Section on Orthopedic Surgery at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 14, 1934.

1. Levinson, Abraham: Cerebrospinal Fluid in Health and in Disease, ed. 1, St. Louis, C. V. Mosby Company, 1919, p. 63.

2. Schmorl, G.: Ueber die an den Wirbelbandscheiben Vorkommenden Ausdehungen und Zerreissungsvorgänge und die dadurch an ihnen und der Wirbelspongiosa hervorgerufenen Veränderungen, Verhandl. d. deutsch. path. Gesellsch. **2**:250, 1927.

3. Keyes, Donald C., and Compere, Edward L.: The Normal and Pathological Physiology of the Nucleus Pulposus of the Intervertebral Disc, J. Bone & Joint Surg. **14**:4, 897 (Oct.) 1932.

4. Billington, R. Wallace: Spondylitis Following Cerebrospinal Meningitis, J. A. M. A. **83**:683 (Aug. 30) 1924.

A series of twelve cases showed a thinning of the intervertebral disks and a definite sclerosis of the vertebral bodies, the results of loss of material from the nucleus and of irritation of the bone, respectively. Five of these twelve cases occurred following the withdrawal of fluid for diagnosis; five occurred following the intraspinal administration of antimeningococcus serum; one, following an encephalogram, and one, following the administration of spinal anesthesia.

In performing lumbar punctures on cadavers it was learned that one cannot determine when the point of the needle is actually in the neural canal. In some cases there was a slight decrease in resistance when the canal was reached, but this occurred only when the needle was

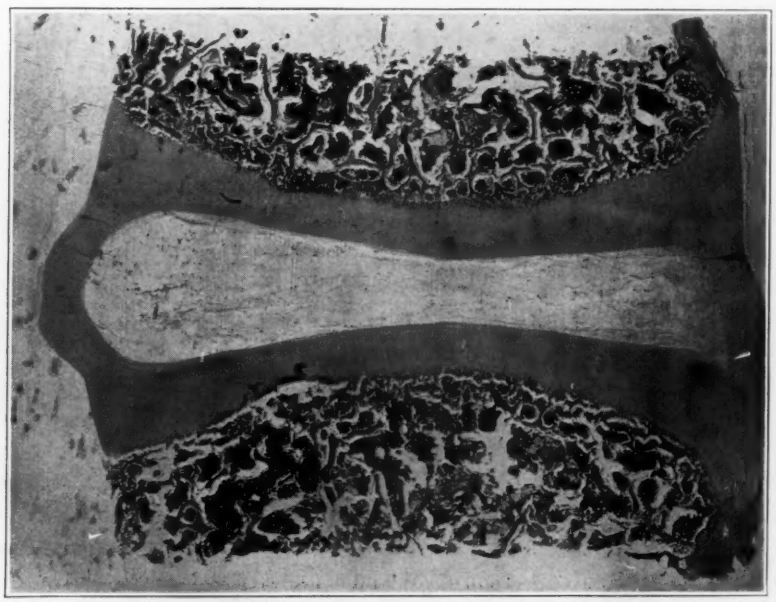

Fig. 1.—Photomicrograph of an intervertebral disk and portions of adjacent vertebrae. Note the thickness of the anterior as compared with the posterior wall. Note also how pressure from above and below causes a bulging posteriorly.

introduced very delicately. However, in the great majority of the cases it was impossible to determine the position of the point of the needle. Similarly, if the needle was pushed in too far, one could not tell when it struck the intervertebral disk and passed into it. On the other hand, it was not difficult to ascertain the situation when the point of the needle struck a bony portion of the vertebra.

Further experimental puncture on cadavers revealed that there were several possible terminations if the needle was pushed beyond the neural canal, the most common sites being: (1) the intervertebral disk, (2) a vertebra, (3) interarticular facets and (4) venous sinusoids in the vertebral body.

ANATOMIC CONSIDERATIONS

Briefly, the intervertebral disk consists of the superior and inferior cartilaginous plates, the annulus fibrosus and the nucleus pulposus. The annulus fibrosus is thicker anteriorly than posteriorly, and this difference,

Fig. 2.—Superior cartilaginous plate removed from an intervertebral disk. Note the swelling of nucleus pulposus from its bed.

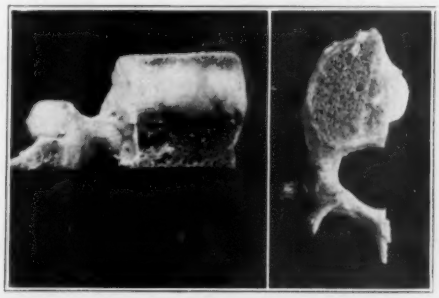

Fig. 3.—Side and top view of sagittal section of an intervertebral disk and portions of adjacent vertebrae. Note the expansion of the nucleus pulposus.

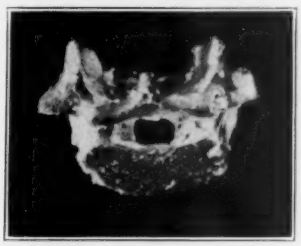

Fig. 4.—Lumbar vertebra showing venous sinusoid in the posterior portion of the body.

together with its close union with the anterior longitudinal ligament, makes the disk much stronger and more powerful in front (fig. 1). The nucleus pulposus which, embryologically, is found by mucoid degeneration of the notochord cells is a translucent, semigelatinous fluid through which are interspersed fine fibrous strands. Although the nucleus

pulposus is a distinct structure and on superficial examination appears to be well demarcated from the annulus fibrosus, a closer examination reveals a gradual blending of the former into the latter.

The nucleus pulposus occupies from one half to one sixth the volume of the intervertebral disk, varying inversely with the age of the person. It is under considerable pressure at all times owing to its own elastic turgor. I shall refer to this tension as "intradisk pressure." Therefore, when the intervertebral disk is split either sagittally or transversely the nucleus swells out of its bed (figs. 2 and 3). If the cut surface is inverted some of the nuclear material drips from the specimen, especially so, if the specimen is taken from a warm cadaver.

In connection with this study mention should be made of the venous sinusoids in the vertebral bodies and their associated veins with special reference to those in the posterior portion (fig. 4). The fact that not enough attention is given to these sinusoids has been emphasized by Wagoner and Pendergrass [5] in relation to other conditions.

Attention is called to the articulations between the superior and inferior articular processes of the vertebral arches. These intra-articular facets are true diarthrodial joints with hyaline cartilage on the apposed surfaces surrounded by joint capsules lined with synovia.

MECHANISM

When the torso is flexed in preparation for a lumbar puncture and the needle inserted in the midline beyond the neural canal it will enter the intervertebral disk. If the body is not flexed the needle will strike the vertebral body or enter the venous sinusoid or one of the connecting veins. Moreover, if the needle is not introduced sagittally it is possible for it to strike the facets.

In flexing the spine the positive intradisk pressure is increased by the closer approximation of the vertebral bodies anteriorly. Because of the stronger anterior elements of the intervertebral disk and the anterior longitudinal ligament the effect of the increased intradisk tension is reflected in the weaker posterior portion. This causes a slight bulging of the disk into the neural canal (fig. 5). The needle, in entering the latter region, allows the nucleus pulposus to escape into the lumen of, or around, the needle.

In addition to the purely mechanical trauma outlined, it is possible for the needle to carry organisms into the intervertebral disk or vertebrae, thus setting up a localized infectious process.

Roentgenograms of the spine taken before and after the introduction of a needle into the disk demonstrate a narrowing of the disk in the latter instance.

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5. Wagoner, George, and Pendergrass, Eugene P.: Intrinsic Circulation of the Vertebral Body, Am. J. Roentgenol. **27**:818 (June) 1932.

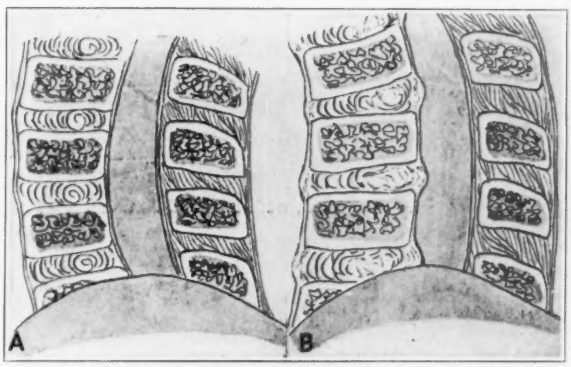

Fig. 5.—*A*, diagrammatic sagittal section of lumbar vertebrae showing normal tension of intervertebral disk and nucleus pulposus. *B*, diagrammatic sagittal section of lumbar vertebrae showing flexion of the spine and increased intradisk pressure. Note the bulging into the neural canal.

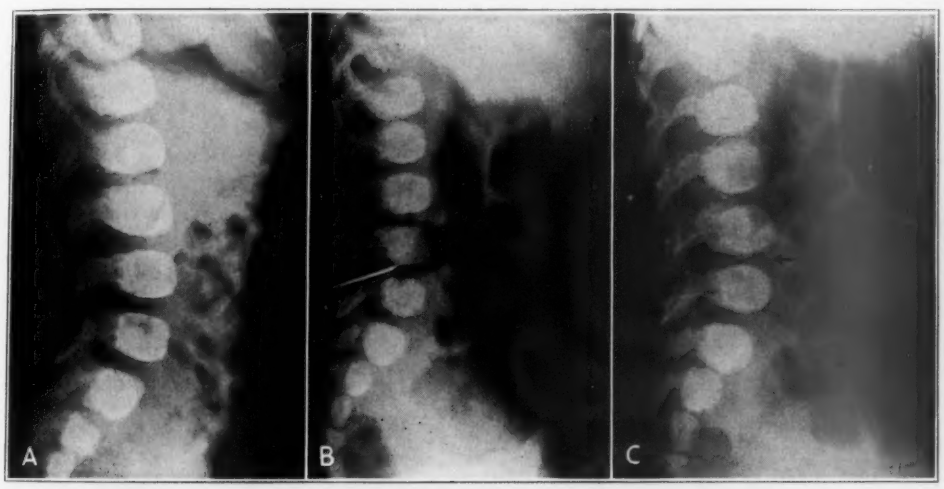

Fig. 6.—*A*, normal lumbar vertebra from a child 2 years of age. *B*, spinal puncture needle penetrating the intervertebral disk between the fourth and fifth lumbar vertebrae. *C*, roentgenogram taken immediately after the withdrawal of the needle. The intervertebral disk between the fourth and fifth lumbar vertebrae is narrowed (1.5 mm. less than on the normal film).

The following clinical case confirms the observations made on the cadaver:

Recently, there came under my observation a child, aged 2 years, who was moribund from miliary tuberculosis and tuberculous meningitis. A roentgenogram of the spine had been taken but revealed no evidence of pathologic changes. A diagnostic lumbar puncture was performed, and while the needle was being introduced a resistance was felt as though the point had struck bone. It was thought that the needle was touching the posterior portion of the body of one of the lumbar vertebrae, and the opportunity was taken to locate the position of the needle by roentgen examination.

By checking the location of the needle in this manner it was discovered that the aforementioned assumption was not correct but that the needle had penetrated the intervertebral disk and was impinged against the inferior border of the fourth lumbar vertebra. The needle was withdrawn, and in its lumen was noted material from the nucleus pulposus; by gross and microscopic examination this material was proved to be mucus.

Roentgen films made immediately following the withdrawal of the needle showed a diminished intervertebral space between the fourth and fifth lumbar vertebrae (fig. 6).

CLINICAL CONSIDERATIONS

Symptoms.—The onset of the symptoms in the twelve cases that form the basis of this study varied from immediately following the puncture to a period of two weeks.

The chief complaint in the cases presented was pain in the lower part of the back, localized at the site of the puncture. Associated with this were limitation of motion of the lumbar spine and weakness of the muscles of the back. In some cases there were night cries. In others difficulty in walking and pain referred down the thighs were present.

The examination revealed a weakness of the muscles in the lower part of the back. Associated with this symptom was an involuntary muscular spasm in that region which limited the motion of the lumbar spine in all directions. There was also a loss of the normal lumbar lordosis, and in some cases an actual rounded kyphosis occurred in this region.

Roentgen Findings.—The roentgen findings varied considerably. The mildest type of lesion demonstrable was a lumbar scoliosis. However, the predominant finding was a thinning of the intervertebral disk between the third and fourth or fourth and fifth lumbar vertebrae. Associated with this was a narrowing of the space between the respective vertebral arches and the interarticular facets, together with sclerosis of the vertebral bodies apparently due to mechanical shock from the lack of the cushion effect of the disk between the bodies. Also, there appeared a complete destruction of the intervertebral fibrocartilage with typical findings of osteomyelitis of the adjacent vertebrae.

In one case, along with the narrowed intervertebral space there was a slight prolapse of the nucleus pulposus into the vertebral bodies as described by Schmorl. In another case there was a small spicule of bone in the neural canal that was attached to the lamina, evidently arising from a periosteal tear. Also, in one case in which there was a considerable loss of intervertebral space between the third and fourth lumbar vertebrae there appeared to be a compensatory widening of the disks between the second and third and the fourth and fifth lumbar vertebrae, respectively.

Treatment.—The treatment varies with the severity of the local symptoms. Simple rest in bed may suffice in mild cases. However, in most of the cases rest in hyperextension on a Bradford frame followed

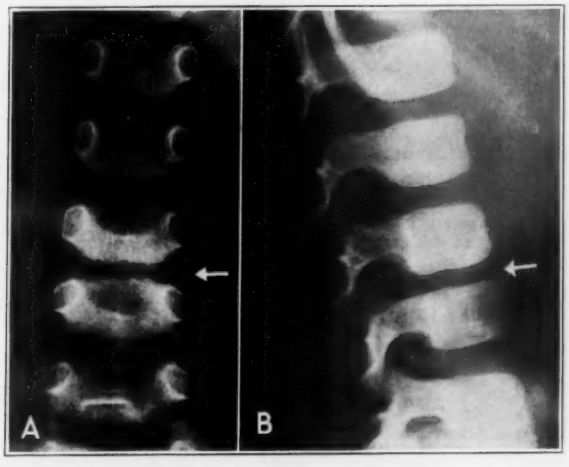

Fig. 7 (case 1).—*A,* narrowing of the intervertebral space between the third and fourth lumbar vertebrae. *B,* narrowing of the space between the vertebral arches of these vertebrae. There is an increased density of the third and fourth lumbar vertebrae.

by the wearing of a plaster jacket or a Taylor brace was necessary. In one case, that of an adult, conservative measures were not sufficient to relieve the pain, and lumbosacral fusion was resorted to (case of Dr. Philip H. Kreuscher).

REPORT OF THREE ILLUSTRATIVE CASES

CASE 1.—J. B., a white boy, aged 4½ years, was admitted to the orthopedic service of Dr. Fremont A. Chandler of the Children's Memorial Hospital on Sept. 5, 1930. Two weeks previously he had undergone lumbar punctures followed by the injection of air into the spinal canal for an encephalogram. A first attempt at this procedure was unsuccessful, so it was repeated two days later. Since the spinal punctures he had complained of pain and stiffness of the back which were associated with night cries.

The patient had had pneumonia at 14 months, followed by monoplegia involving the left leg. Following this he had chickenpox and bilateral otitis media. The father had died of pulmonary tuberculosis.

An examination of the patient's back revealed rigidity of the lumbar spine. There was some restriction of internal rotation of both femurs. Spasm of the iliopsoas muscle was present.

Anteroposterior and lateral roentgenograms of the spine showed a thinning of the intervertebral disk between the third and fourth lumbar vertebrae. Four months later both of these vertebrae showed a slight sclerosis of their bodies (fig. 7).

Fig. 8 (case 2).—Narrowing of the intervertebral disk and marked proliferation and sclerosis of vertebrae, a true osteomyelitis. There is also a slight lateral displacement of the third lumbar vertebra on the fourth. Note the compensatory widening of the remaining intervertebral space in the lumbar region.

CASE 2.—F. H., a white boy, aged 10 years, was admitted to the Children's Memorial Hospital on June 3, 1927. The mother stated that on March 25 the child had epidemic meningitis. A spinal puncture was made by the family physician at that time, and the child was sent to the hospital for contagious diseases. There another puncture was made and antimeningococcus serum was given intraspinally. Recovery was uneventful, and the patient was discharged on May 3. Forty-eight hours later he had a relapse with fever, headache, vomiting and marked opisthotonos. He was returned to the hospital for contagious diseases where another spinal puncture was made and serum administered. During his recovery he com-

plained of pain and stiffness in the lower part of the back He was transferred to the Children's Memorial Hospital for diagnosis and treatment. The past history was essentially irrelevant.

The physical examination revealed no positive findings with the exception of those present in the back. A few pinpoint scars were present in the skin in the midline of the lower part of the back. The normal degree of lumbar lordosis was diminished. Motion of the lumbar spine was limited in all directions.

Anteroposterior and lateral roentgenograms of the spine revealed a partial destruction of the third and fourth lumbar vertebrae with an increased sclerosis of these segments. The fourth lumbar vertebra was displaced slightly to the right. The anteroposterior diameters of these vertebrae were increased. There was almost a complete loss of the intervertebral disk between the third and fourth lumbar vertebrae.

The patient was placed on a Bradford frame for three months; then he was allowed up wearing a plaster jacket for a similar length of time, after which support was removed entirely. Although motion in the lumbar region remained restricted he had no further symptoms (fig. 8).

CASE 3.—J. T., a boy, aged 6 years, was admitted to my private service at the Children's Memorial Hospital on Nov. 24, 1930. He had had acute anterior poliomyelitis three months previously. At the time this diagnosis was made he was anesthetized, and spinal puncture was attempted, but on several insertions of the needle no fluid was obtained. He was kept in bed. About a month later he began to have pain in the lower part of the back and on the right side. The mother stated that it was thought he had pyelitis. He began to have night cries every night. This continued and was still present at the time of admission. The past history and the family history were essentially irrelevant.

Examination at the time of admission revealed a fairly well nourished child of 6. Examination of the back showed a spasm of the lumbar muscles and a loss of the normal lumbar lordosis. Motions of the lower half of the spinal column were limited in all directions. Both psoas muscles were in spasm.

Anteroposterior and lateral roentgenograms of the spine showed a decrease in the intervertebral space between the fourth and fifth lumbar vertebrae. There was also an increased density of the fourth lumbar vertebra.

COMMENT AND CONCLUSION

Although I could have reported in detail several additional cases which were offered to me by many of my colleagues, I have chosen to report only those which have come under my personal observation or in which the patients were cared for by a few of my colleagues in Chicago, merely to demonstrate that these lesions are much more common than is ordinarily suspected.

The purpose of this report is in no way to discourage lumbar puncture, but rather to call attention to the newly described complications which may be added to the already long list of accidents resulting from the withdrawal of spinal fluid.

From the foregoing one can conclude that in performing a lumbar puncture it is possible, unknowingly, to introduce the needle too far, penetrating the intervertebral disk or the vertebra. The sequelae from

this may be a narrowing of the intervertebral space which can be demonstrated by roéntgenograms. Various types of inflammatory reactions may be set up in the bony and articular elements of the spine.

ABSTRACT OF DISCUSSION

DR. EDWARD L. COMPERE, Chicago: In studies of the intervertebral disk the interesting possibility presented by Dr. Pease has been entirely overlooked. The danger of injury to the intervertebral disk by the lumbar puncture needle is much greater in young children than in adults. The interesting and important studies of Dr. Pease dealt mostly with children. In the child about two thirds of the intervertebral disk is composed of the semigelatinous rather viscid material of the nucleus pulposus which is not exactly fluid but which can be expressed and is under sufficient pressure from the vertebral bodies above and below the ligaments to be forced out if a sufficient opening is made.

In some experimental work with dogs in an attempt to measure the pressure of the nuclear material, my associates and I were unable to insert a needle large enough to cause the semigelatinous substance to rise in the needle and register the pressure. This indicated that the substance is not easily expressed through a small opening.

The following slides may help to illustrate this point (demonstration of slides).

This slide represents a dog's spine. It shows two intervertebral disks injured shortly before this spine was obtained by the passing of the narrow blade of a scalpel through the annulus fibrosus. In a dog, even in an adult dog, the nuclear material is more fluid than it is in a 10 year old child. The younger the child, the greater the water content. As the person grows older, the disk becomes more and more dehydrated, and it is difficult to express any fluid from the disk of a middle-aged patient even though the annulus is cut all around.

The second slide shows what Dr. Pease pointed out, that on the side of the spinal canal, the side that can be entered by an exploring needle, the annulus fibrosus is thinner than it is on the opposite side.

The third slide illustrates how much of the intervertebral disk is nuclear material in a 14 month old child. The nuclear material occupies most of the intervertebral space. As the child grows older the fibrous tissue growing in increases until by the time the person is from 40 to 60 years of age there is considerable fibrous tissue and the capsule has become enormously thickened.

The next slide shows a dog's spine in which a scalpel was introduced through the annulus fibrosus. In less than three months all the nuclear material was gradually expressed. Not very much comes out immediately at the time of injury, but if the animal is allowed to be active there is further extrusion of the nuclear material. When this hydrodynamic ball-bearing action is lost from between the vertebrae, the fibrous portion of the intervertebral disk wears out in the same way as shoe leather. In the spine illustrated here it has disappeared, and the hyaline cartilage which covers the cortical portion of the vertebral bodies has likewise been eroded, exposing cortical bone.

This slide merely illustrates one of several cases examined at autopsy. It shows the extrusion into and the formation of a nodule in the spinal canal and the narrowing of the disk.

I am inclined to believe that in the cases in adults which Dr. Pease cited the pathologic changes in the disk may have been the reason for the spinal puncture and not a result of it.

DR. C. G. BARBER, Cleveland: It would be difficult to estimate with any degree of accuracy the number of lumbar punctures that have been performed in the past forty-nine years (Corning, James Leonard: Spinal Anesthesia and Local Medication of the Cord, *New York State J. Med.* **42**:483 [Oct.] 1894). Early papers advocated its adoption as a diagnostic and therapeutic measure and pointed to its safety and harmlessness, except in some cases of hydrocephalus and tumor of the brain. Dr. Pease's report together with his exhibit add, as he has stated, "new complications to the already long list of accidents resulting from the withdrawal of spinal fluid."

There were several things mentioned in Dr. Pease's paper about which I should like to have a clearer understanding: 1. At what point was the needle inserted so as to strike the interarticular facet when the needle was pushed beyond the neural canal?

2. How was the thickness of the disks determined? My reason for asking this question is that in thirty-three vertebral columns, each of twenty-four presacral vertebrae obtained from white men patients, Todd and Pyle (Todd, T. W., and Pyle, S. I.: A Quantitative Study of the Vertebral Column by Direct and Roentgenoscopic Methods, *Am. J. Phys. Anthropol.* **12**:321 [Oct.-Dec.] 1928) found the vertical dimension of intervertebral disks to vary from 8 to 19 mm. The disk between the second and third lumbar vertebrae averaged 11.3 mm. with a range of from 8 to 14 mm.; the disk between the third and fourth lumbar vertebrae averaged 12.4 mm., with a range from 8 to 16.5 mm., and the disk between the fourth and fifth lumbar vertebrae averaged 14.8 mm., with a range from 11 to 19 mm. Todd and Pyle also found that a lateral roentgenogram gave the measurement of a disk, but that an anteroposterior roentgenogram did not. They also found that successive roentgenograms must be centered in exactly the same manner.

3. Just what is meant by compensatory widening of the disks?

4. In regard to case 1, is not two weeks a rather short time for the development of a sclerosis far enough advanced to show on a roentgenogram?

5. One other thing which was not quite clear to me was that case 2 showed an osteoporosis of the third and fourth lumbar vertebrae; others, for example case 3, showed an osteosclerosis.

DR. L. E. PAPURT, Cleveland: I should like to ask Dr. Pease about the prolapse he said he had observed in one of these cases. I do not see how that came about.

DR. E. BENNETTE HENSON, Charleston, W. Va.: The condition described by Dr. Pease has definite practical application. Two years ago a soldier applied for compensation for spinal arthritis as a result of repeated spinal punctures which he had undergone for meningitis while he was in the army. I could find no reference in the literature in this connection, but I recalled that in 1917 Dr. Robert W. Lovett demonstrated such a case, and for that reason the soldier's claim was held to be valid.

DR. CHARLES N. PEASE, Chicago: In reply to Dr. Barber, I should like to state that if the needle is put in at an angle it may strike the facet. Some physicians perform their lumbar punctures from the side instead of straight in.

The distance between the vertebrae and the thickness of the intervertebral disk may vary, but I think that a comparison of the disks shown with the ones above and below together with the experimental work, the report of the clinical case, the history that there had been no disability of the back previous to the lumbar puncture,

the signs of spinal irritation and the findings of a narrowed disk on roentgen examination should be sufficient to make a diagnosis of narrowing of the disk due to the lumbar puncture.

Compensatory widening is speculative. I believe that, owing to the great amount of pressure of the nucleus pulposus, there is a simultaneous widening or expansion of the intervertebral disks as the disk above or below becomes narrower.

The prolapse into the body is explained by the fact that the needle could penetrate the superior plate of the intervertebral disk and that the nucleus pulposus could exude into the body through that little hole in the superior plate.

I wish to add that when the nuclear material is lost, it is not replaced, because the nucleus pulposus is derived from embryonic cells of the notochord, and when that is gone it is beyond recall.

BODY BUILD IN INFANTS

VI. GROWTH OF THE CARDIAC SILHOUETTE AND THE THORACO-ABDOMINAL CAVITY

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Our aim in the present study was to determine some of the changes which occur in the size and shape of the cardiac silhouette and the thoraco-abdominal cavity from birth until the end of the first year and to define their relations to some of the external body dimensions. Measurements of the heart and thoraco-abdominal cavity were made from roentgenograms. The external dimensions were measured by a technic previously described.[1] Means and standard deviations, which measure the extent of departures from the mean, were calculated.

MATERIAL AND METHOD

The infants used in this study (165 boys and 146 girls) were born in Bellevue Hospital and came for the most part from very poor homes. After being discharged from the maternity wards, they were supervised in a special clinic devoted to the care of well infants. These infants grew normally, averaging 739 mm. in height and 9,500 Gm. in weight at the end of the first year. Only infants of Caucasian antecedents were studied.

Roentgenologic Technic.—Anteroposterior roentgenograms of the thorax and abdomen were taken at a distance of 2 meters, with the infants supported in the sitting posture by the device described by Wimberger.[2] Two roentgenograms were taken of each infant, and the better one was used for making measurements. No attempt was made at timing according to the phase of respiration.

Dr. Paul T. Meyers took the roentgenograms used in this study.

Dimensions Measured (fig. 1).—The cardiac dimensions were measured in the usual manner.

Read before the Heart Committee of the New York Tuberculosis and Health Association, April 24, 1934.

From the Department of Diseases of Children, New York University and Bellevue Hospital Medical College, and the Children's Medical Service, Bellevue Hospital.

1. Bakwin, H., and Bakwin, R. M.: Body Build in Infants: I. The Technique of Measuring the External Dimensions of the Body in Infants, J. Clin. Investigation **10**:369, 1931.

2. Wimberger, H.: Technische Erfahrungen aus der Kinderröntgenologie, Fortschr. a. d. Geb. d. Röntgenstrahlen **24**:96, 1922.

The area of the thoracic cavity, bounded laterally by the ribs and intercostal tissues, above by a line connecting the lateral arches made by the ribs and below by the dome of the diaphragm, was measured with the planimeter.

The area of the abdominal cavity, bounded above by the dome of the diaphragm, laterally by the abdominal wall and below by an arc through the crests of the ilia, not including the pelvic cavity, was measured with the planimeter.

The length of the abdomen was measured from the dome of the diaphragm to the lower margin of the abdominal cavity in the midline.

The length of the thorax was measured from the dome of the thoracic cavity to the level of the dome of the right leaf of the diaphragm in the midline.

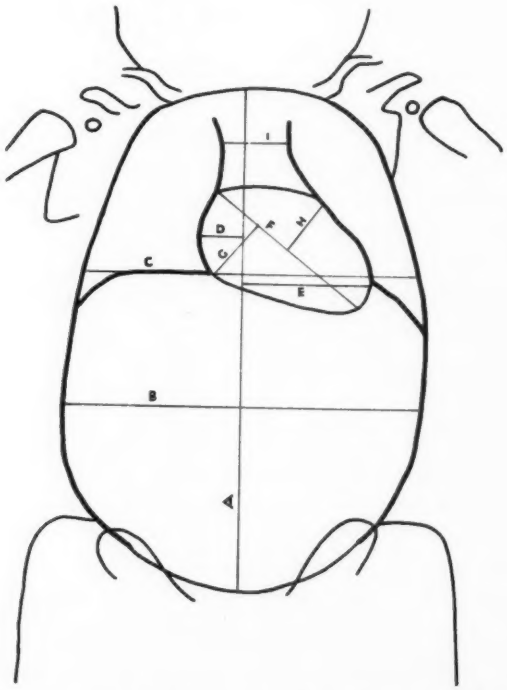

Fig. 1.—The cardiothoracic cavity and cardiac silhouette of an infant at birth, showing the dimensions measured. *A* represents the length of the thoraco-abdominal cavity, *B*, the width of the abdomen, *C*, the width of the thorax, *D*, and *E*, the transverse diameter of the heart, *F*, the long diameter of the heart, *G* and *H*, the broad diameter of the heart, and *I*, the diameter of the mediastinum.

The width of the abdomen was measured on the greatest diameter of the abdominal cavity, perpendicular to the thoraco-abdominal length.

The width of the thorax was measured from one lateral wall of the thoracic cavity to the other, tangent to the dome of the right leaf of the diaphragm and perpendicular to the thoraco-abdominal length.

The diameter of the mediastinum was measured from the right to the left border of the mediastinal shadow in the second intercostal space, perpendicular to the thoraco-abdominal length.

Reliability of Measurements.—A test of the reliability of the roentgenologic technic in infancy was made by correlating the measurements of the transverse diameter of the heart in duplicate roentgenograms of 36 infants in the age period of from 32 to 39 weeks. The high coefficient of correlation obtained (0.89) indicates a high degree of reliability.

ANATOMY AND MEASUREMENTS OF THE HEART AND THYMUS DURING INFANCY

At birth the heart weighs from 20 to 25 Gm.[3] The left ventricle constitutes a larger proportion of the anterior surface than it does in adult life. Only the ventricles are in contact with the anterior wall of the chest, the auricles being covered by the thymus. The conus arteriosus is bent dorsally more than in the adult, and the auricles are larger in relation to the ventricles.[4] The apex is more rounded, and the maximum apical impulse which is felt in the fourth intercostal space outside the mammary line does not correspond to the anatomic apex, which is ordinarily in the fifth intercostal space.[3a]

At birth the left ventricular wall weighs about 25 per cent more than the right wall and is about 50 per cent thicker. It grows much more rapidly than the right, however, doubling its weight at birth by the fourth to the fifth month, during which time the right ventricle grows only about 20 per cent.[5] At the end of the first year the left ventricle is about two and one-half times the thickness of the right. According to Scammon,[3b] the weight of the heart increases about 100 per cent during the first year, while the body weight is tripled.

The first extensive roentgen study on infants was that of Bamberg and Putzig,[6] in 1919; these authors presented data on over a hundred roentgenograms of infants under 1 year of age and correlated their results with age, total body length and sitting height. The infants whom they used were considerably retarded in growth of weight and total body length, the average weight of the group at 1 year being about 7,600 Gm. After the first month of life the cardiac dimensions were regularly smaller than those for our group. Measurements of the dimensions of the cardiac silhouette have been reported by Voss,[7] Lehm-

3. (*a*) Gräper, L., in Peter, K.; Wetzel, G., and Heiderich, F.: Handbuch der Anatomie des Kindes, Munich, J. F. Bergmann, 1928, vol. 1, p. 293. (*b*) Scammon, R. E.: Studies on the Growth and Structure of the Infant Thorax, Radiology **9**:89, 1927.

4. Müller, W.: Die Massenverhältnisse des menschlichen Körpers, Leipzig, L. Voss, 1883.

5. Falk, A. A.: Das Wachstum des Herzens bei Kindern, Dissert., St. Petersburg, 1901; quoted by Gondobin, N. P.: Die Besonderheiten des Kindesalters, Berlin, S. Rubinstein, 1913. Scammon.[3b]

6. Bamberg, K., and Putzig, H.: Die Herzgrösse im Säuglingsalter auf Grund von Röntgenfernaufnahmen, Ztschr. f. Kinderh. **20**:195, 1919.

7. Voss, E.: Röntgenographische Grössenbestimmungen des Herzens im Säuglings- und Kleinkindesalter, Ztschr. f. Kinderh. **48**:428, 1929.

kuhl,[8] Baccichetti [9] and Farrell.[10] An excellent summary was given by Brock.[11]

OBSERVATIONS ON RESULTS OF MEASUREMENTS

Growth of the Cardiac Silhouette in the Normal Infant.—Changes in the size of the cardiac silhouette, though due mainly to the increase in size, depend also on the change of position of the heart and on the increasing technical distortion. As the infant grows the heart becomes more linearly placed, thus tending to diminish the transverse diameter. This change in the angulation of the cardiac silhouette results in a diminution of the transverse diameter amounting to about 7 per cent. During infancy the heart usually lies anterior to the fifth to the ninth or tenth dorsal vertebra. It is ordinarily globular at birth, the

TABLE 1.—*Dimensions of the Cardiac Silhouette and the Thoraco-Abdominal Cavity in Normal Infants by Certain Subdivisions of Age Under 1 Year*

Age, Mos.	Area of Heart, Sq.Cm. (S.D.*, 4.5)	Transverse Diameter of Heart, Mm. (S.D., 6)	Long Diameter of Heart, Mm. (S.D., 7.5)	Heart Angle, Degrees (S.D., 6)	Diameter of Mediastinum, Mm. (S.D., 6.2)	Area of Thoracic Cavity, Sq.Cm. (S.D., 12.5)	Length of Thorax, Mm. (S.D., 8)	Width of Thorax, Mm. (S.D., 8)	Area of Abdominal Cavity, Sq.Cm. (S.D., 17.5)	Length of Abdomen, Mm. (S.D., 11.5)	Width of Abdomen, Mm. (S.D., 7.5)
Birth	14	49	54	32	26	40	51	90	94	106	99
1	18	54	59	33	29	43	55	95	102	110	107
2	21	58	63	33	31	48	60	101	109	115	113
3	23	61	67	33	32	55	64	106	118	118	118
4	26	64	70	34	32	61	67	111	124	122	122
5	28	66	73	34	33	67	71	116	132	124	127
6	30	68	75	34	33	73	74	121	140	127	131
7	31	70	77	35	33	78	76	125	147	129	134
8	33	72	79	35	33	82	79	129	155	132	138
9	34	73	80	36	32	85	81	131	159	135	140
10	35	74	81	36	32	88	83	133	163	137	142
11	35	74	81	37	32	90	84	135	166	138	144
12	36	75	82	38	32	92	85	137	169	140	144

* S.D. means standard deviation.

left border being smoothly convex and the left auricle and pulmonary artery not being clearly demarcated. Later in infancy it is generally possible to distinguish these divisions. Occasionally the pulmonary conus is prominent.

The averages and standard deviations for the dimensions measured were calculated by eight subdivisions of age under 1 year. The data for both sexes were combined. The averages for the boys were regularly larger than those for the girls. The data shown in table 1 were

8. Lehmkuhl, H.: Röntgenologische Untersuchungen des Herzens im Kindesalter, Jahrb. f. Kinderh. **123**:66, 1929.

9. Baccichetti, A.: Atti d. congr. pediat. ital., 1925, p. 211; abstr., Zentralbl. f. Kinderh. **19**:548 and 549, 1925-1926.

10. Farrell, J. T.: The Roentgen Appearance of the Chest of the New-Born Infant, Am. J. Roentgenol. **24**:140, 1930.

11. Brock, J.: Biologische Daten für den Kinderarzt, Berlin, Julius Springer, 1932, vol. 1.

obtained by fitting graphically a smooth curve to the observed averages. The values so obtained probably represent more accurately the growth of the various dimensions than do the observed averages.

At birth the silhouette of the heart is more transversely placed than in later life, the heart angle being about 32 degrees; the right side is relatively large, the right diameter being about 56 per cent of the left. The heart is broad relative to the width of the chest.

During the first year the heart grows rapidly, the frontal plane more than doubling in area. A measure of the rapidity of the growth during

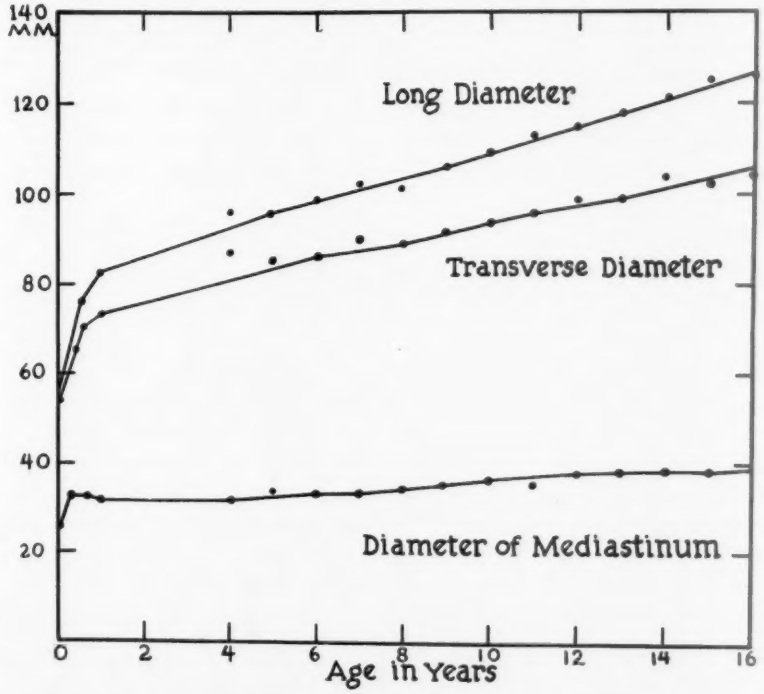

Fig. 2.—Growth of various dimensions of the cardiac silhouette from birth to the age of 16 years. The data after the first year are from Ziskin.[12]

this age period may be gained from figure 2, in which the growth of various dimensions from birth until 16 years of age is illustrated. The data for growth after the first year are those of Ziskin.[12] The heart angle increases to 38 degrees, but is still considerably smaller than the angle in the adult. The relation of the right diameter to the left remains unchanged. The changes in the shape of the heart from birth until the

12. Ziskin, T.: Development and Size of the Heart in Children, Am. J. Dis. Child. **30**:851 (Dec.) 1925.

age of 16 years are illustrated in figure 3. The dimensions at 5 years and at 16 years are after Ziskin.[12]

The variability[13] of the transverse diameter during infancy (from 7 to 11 per cent) is somewhat larger than in childhood (from 5 to 8 per cent).[14] The variability is greater during the earlier than during the later weeks of the first year.

The most variable cardiac dimension during infancy is the frontal plane area (from 15 to 20 per cent variation). Though this is probably due partly to the indefiniteness of the upper and lower margins of the cardiac silhouette, which are arbitrarily drawn in, it seems hardly likely that this is the sole factor. The long and broad diameters of the heart show about the same percentage of variability as the transverse diameter.

Diameter of the Mediastinum.—At birth the mediastinum is broad in relation to the cardiac silhouette. Its diameter increases until about the twentieth week, after which it gradually diminishes. An increase in

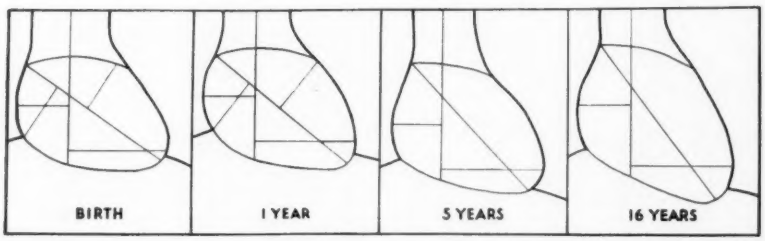

Fig. 3.—Shape of the cardiac silhouette at various age periods from birth to the age of 16 years. The transverse diameter of the heart is constant. The data after the first year are from Ziskin.[12]

the weight of the thymus during the first weeks of life, followed by a decrease, has been noted by a number of observers.[15] At the end of the first year the mediastinum is narrower relative to the cardiac silhouette than it was at birth, but is still relatively broader than it is in adult life.

The variability of its diameter is large (about 20 per cent) throughout most of the first year. The distribution for the new-born—the largest group studied—is normal.

The Thoraco-Abdominal Cavity.—The frontal plane of the thorax more than doubles in area during the first year of life, while the abdominal area increases only about 70 per cent. The relatively small

13. The variability, i. e., the coefficient of variation, of a dimension is equal to one hundred times the standard deviation divided by the average.

14. Lincoln, E. M., and Spillman, R.: Studies on the Hearts of Normal Children, Am. J. Dis. Child. **35**:791 (May) 1928.

15. Boyd, E.: Growth of the Thymus, Am. J. Dis. Child. **33**:867 (Jan.) 1927.

thorax of the young infant is striking. The thoraco-abdominal length grows at about the same rate as the total body length.

The dimensions of the thoracic area are highly variable (the variability is about 20 per cent during the first half year, after which it decreases); those of the abdominal cavity are less variable (from 10 to 15 per cent variability). After the first few weeks of life the width of the thorax and length of the thoraco-abdominal cavity show a variability of about from 5 to 7 per cent.

Relation of the Transverse Diameter of the Heart to the Width of the Thorax.—During the first days of life the transverse diameter of the heart is about 55 per cent of the thoracic width. The proportion increases to about 58 per cent during the second four weeks, after which it decreases gradually to about 53 per cent at the end of the first

TABLE 2.—*The Cardiothoracic Ratio in Infants by Certain Subdivisions of Age Under 1 Year*

Age Range, Weeks	Normal Infants			Undernourished Infants		
	No. of Cases	Mean, Mm.	Standard Deviation, Mm.	No. of Cases	Mean, Mm.	Standard Deviation, Mm.
0 to 3	52	55.31	4.94	..	.....	....
4 to 7	36	57.61	6.02	38	53.42	4.70
8 to 15	71	56.75	5.67	70	54.32	5.10
16 to 23	42	56.67	5.56	42	53.76	5.48
24 to 31	27	55.81	5.53	28	52.64	5.08
32 to 39	35	55.97	4.95	21	53.95	4.77
40 to 47	19	54.37	5.24	10	52.89	5.66
48 to 55	22	52.64	4.31	20	52.80	3.40

year. This is considerably higher than during later childhood or in adult life, when the relationship is about from 40 to 49 per cent.[16]

The relatively large transverse diameter of the heart in infancy is due to its transverse position. If the heart, which lies at an angle of 32 degrees in the thorax of the new-born infant, were tilted up to the angle in the average adult (45 degrees), the transverse diameter would be shortened from 49.7 to 41.4 mm., and the cardiothoracic ratio would be 46, approximating the ratio for adults, which varies from 40 to 50.[17]

The cardiothoracic ratio has been widely used as a measure of the normality of the size of the heart in adults. The variability of this ratio, shown by certain subdivisions of age under 1 year in table 2, is about 10 per cent throughout the first year. This ratio is about as

16. Danzer, C. S.: The Cardio-Thoracic Ratio, an Index of Cardiac Enlargement, Am. J. M. Sc. **157**:513, 1919. Lincoln and Spillman.[14]

17. Eyster, J. A. E.: Estimation of Transverse Cardiac Diameter in Man, Arch. Int. Med. **37**:707 (May) 1926.

variable as that of the transverse diameter of the heart to age, without consideration of the thoracic width (from 7 to 11 per cent variability), and is therefore not much more valuable in judging the normality of the size of the heart in infants than is the size of the transverse diameter itself.

Relation of the Transverse Diameter of the Heart to the Total Body Length.—Throughout the first year of life the transverse diameter of the heart is about 10 per cent of the total body length. The variability of the transverse diameter of the heart by certain subdivisions of the total body length during this age period is over 10 per cent. It is therefore more preferable to relate the transverse diameter of the heart to age than to the total body length.

Relation of the Transverse Diameter of the Heart to the Body Weight.—The variability of the transverse diameter of the heart for

TABLE 3.—*Correlation of the Transverse Diameter of the Heart and Various Body Dimensions at Two Age Periods During Infancy*

	Age, Birth to 3 Weeks (50 Cases)	Age, 32 to 39 Weeks (33 Cases)
Total body length	0.311 ± 0.086	0.105 ± 0.116
Sitting height	0.281 ± 0.088	.....
Body weight	0.244 ± 0.090	0.233 ± 0.111
Circumference of thorax at nipples	0.261 ± 0.089	.....
Internal diameter of thorax	0.498 ± 0.072	0.321 ± 0.105
Biacromial diameter	0.228 ± 0.090	.....
Bimalar diameter of face	0.218 ± 0.091	.....
Square root of heart area	0.763 ± 0.062	.....

certain subdivisions of weight in infancy is about 10 per cent. It is therefore no more useful as a base-line for measuring the normality of the size of the heart than is age or the total body length.

Coefficients of Correlation.—In table 3 coefficients of correlation are presented for the transverse diameter of the heart and various body dimensions in infants of two age periods: less than 4 weeks and from 32 to 39 weeks. From these figures it appears that the transverse diameter of the heart of infants is poorly, if at all, correlated with the total body length, sitting height, body weight, biacromial diameter or bimalar diameter of the face. There is a slight and probably significant correlation with the width of the thorax.

In adults Eyster [17] found a low order of correlation (0.214 ± 0.072) between the transverse diameter of the heart and the total body weight. There was closer correlation with the weight (0.574 ± 0.050). The thoracic dimensions were poorly correlated with the transverse diameter of the heart.[18]

18. Eyster, J. A. E.: Determination of Cardiac Hypertrophy by Roentgen-Ray Methods, Arch. Int. Med. **41**:667 (May) 1928.

SUMMARY

The dimensions of the cardiac silhouette and the thoraco-abdominal cavity, by certain subdivisions of age under 1 year, were measured and means and standard deviations calculated.

The changes in the shape and size of the cardiac silhouette and the thoraco-abdominal cavity during the first year of life are described.

It was observed that the transverse diameter of the heart during infancy is poorly correlated with height, weight and the width of the thorax.

BODY BUILD IN INFANTS

VII. EFFECT OF RETARDED GROWTH ON THE DIMENSIONS OF THE CARDIAC SILHOUETTE AND THE THORACO-ABDOMINAL CAVITY

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In the course of a study on the relation of body form to the incidence of disease it was found that retardation of growth, presumably due to inadequate diet, results in a change in the configuration of the body, undernourished infants assuming different body proportions than better nourished infants from the same social environment.

The purpose of this study was to ascertain the influence of retarded growth on the size and configuration of the cardiac silhouette and the thoraco-abdominal cavity during infancy. If physical constitution is related to the incidence of disease it seems reasonable to assume that the configuration of the internal organs is at least as important as the external body form.

Data are presented on 234 undernourished infants, and the results are compared with similar data on healthy infants given in our preceding paper.[1] The two groups were studied simultaneously.

The undernourished group consisted of infants admitted to the wards of the hospital as healthy boarders or because of mild infections of the upper respiratory tract. In contrast with the group described in the previous paper, they had no regular supervision before admission. They were retarded in growth of weight and total body length and showed changes in the proportions of the external body dimensions.[2]

The technic of taking the roentgenograms and making the measurements was identical with that described in the preceding paper.[1]

Read before the Heart Committee of the New York Tuberculosis and Health Association, April 24, 1934.

From the Department of Diseases of Children, New York University and Bellevue Hospital Medical College, and the Children's Medical Service, Bellevue Hospital.

1. Bakwin, H., and Bakwin, R. M.: Body Build in Infants: VI. Growth of the Cardiac Silhouette and the Thoraco-Abdominal Cavity, Am. J. Dis. Child., this issue, page 861.

2. Bakwin, H., and Bakwin, R. M.: Body Build in Infants: II. The Proportions of the External Dimensions of the Healthy Infant During the First Year of Life, J. Clin. Investigation **10**:377, 1931. Bakwin, H.; Bakwin, R. M., and Milgram, L.: Body Build in Infants: IV. The Influence of Retarded Growth, Am. J. Dis. Child. **48**:1030 (Nov.) 1934.

In charts 1, 2 and 3 the growth curves for various dimensions of the infants in the two groups are compared. Charts 4, 5 and 6 represent the relation of the various dimensions to the total body length and were constructed by plotting the average for the total body length and the dimension in question by certain subdivisions of age under 1 year.

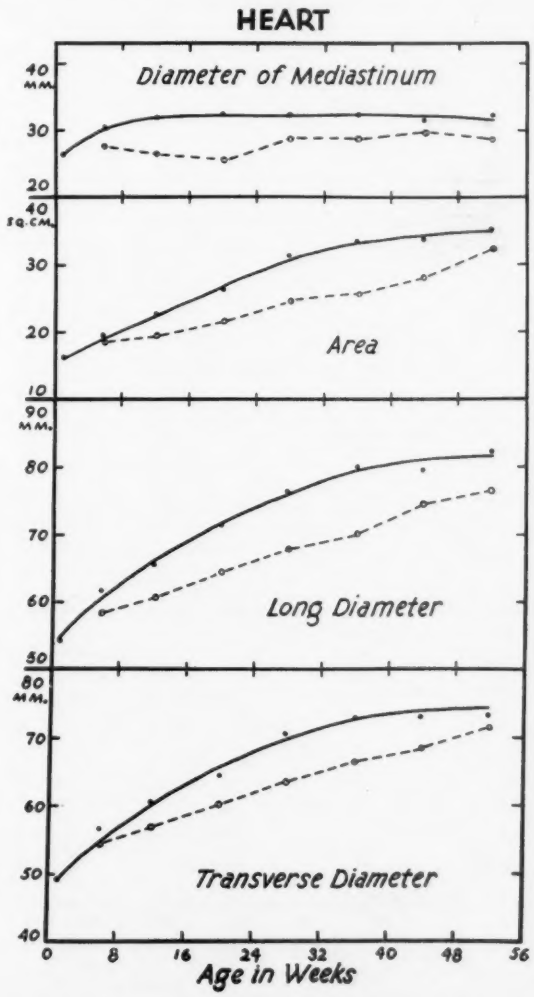

Chart 1.—Growth of various cardiac dimensions and the diameter of the mediastinum in well nourished and undernourished infants by certain subdivisions of age under 1 year. In this and the following charts the dots represent the averages for the healthy infants, and the circles connected by broken lines, the averages for the undernourished infants. The continuous lines are the growth curves for the healthy infants and were constructed graphically to fit the dots.

The cardiac silhouette of the malnourished infant grows more slowly in all its dimensions than that of the better nourished infant. The frontal plane area is consistently smaller, at some age periods (from 24 to 31 weeks) being less than 80 per cent of the area of the supervised

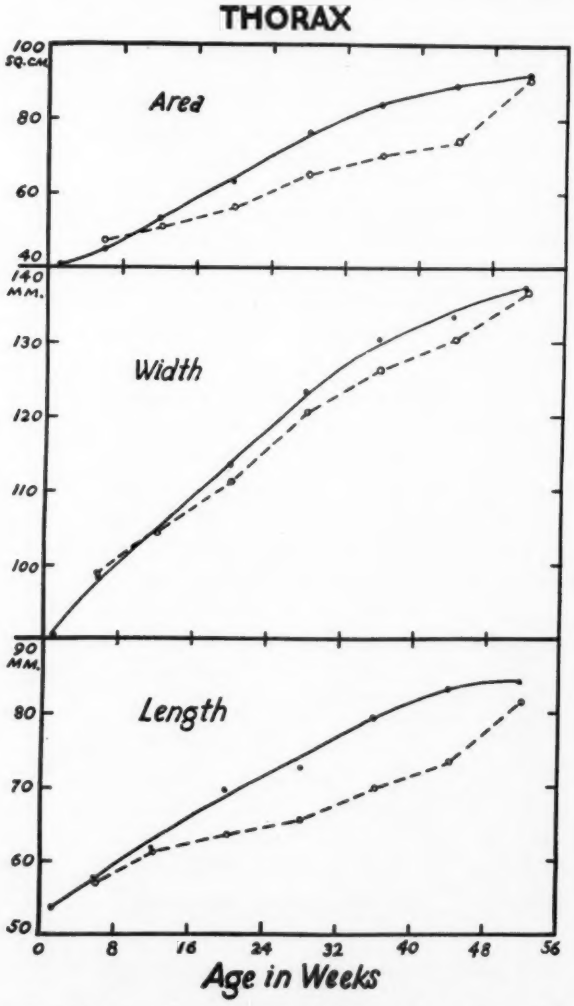

Chart 2.—Growth of various thoracic dimensions in well nourished and undernourished infants by certain subdivisions of age under 1 year.

group of well nourished infants. The heart angle is also smaller, so that the heart is more transversely placed. Since the thoracic length is shorter the heart is higher.

In relation to the total body length the cardiac dimensions are consistently smaller than those of the well nourished infants (chart 4).

The transverse diameter of the heart is consistently smaller in relation to the width of the thorax in the malnourished than in the well nourished infants.

There is a delay in the growth of the mediastinal diameter, in relation both to age and to the total body length.

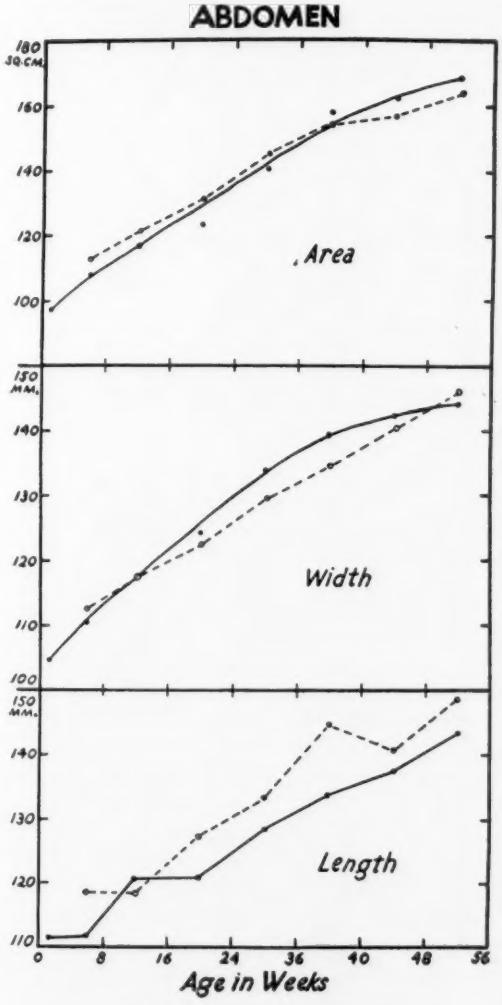

Figure 3

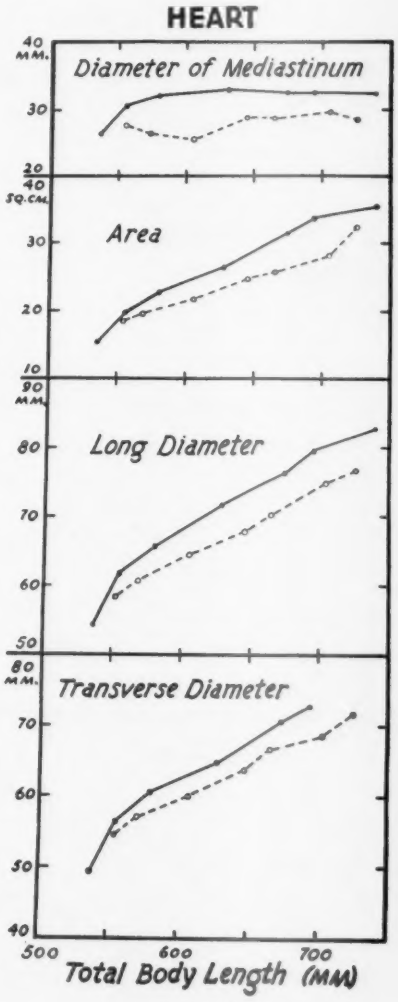

Figure 4

Chart 3.—Growth of various abdominal dimensions in well nourished and undernourished infants by certain subdivisions of age under 1 year.

Chart 4.—Relation of various cardiac dimensions and the diameter of the mediastinum to the total body length in well nourished and undernourished infants under 1 year.

The reliability of the difference in the transverse and long diameters of the cardiac silhouette and in the diameter of the mediastinum of the 2 groups relative to the total body length is shown in the table.

The thoracic dimensions grow more slowly in the undernourished than in the healthy infant. The thoracic area and length are also smaller

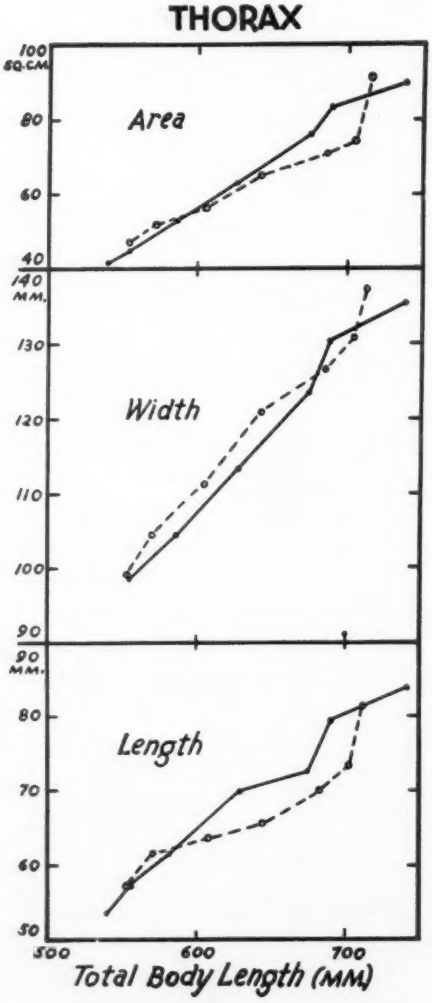

Figure 5

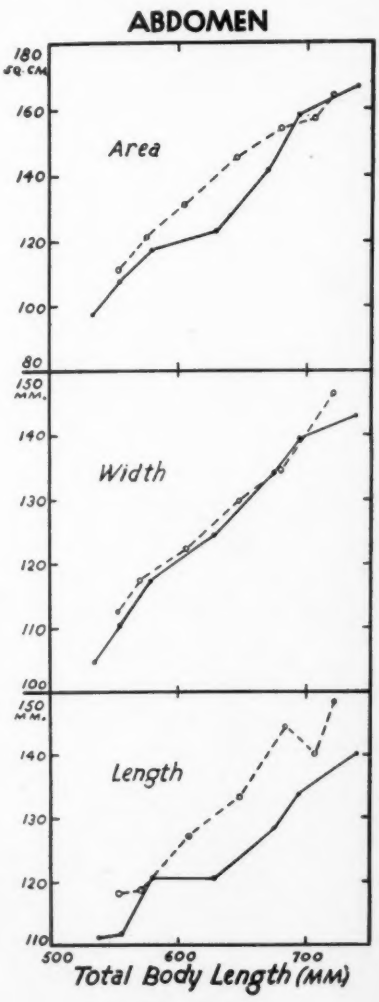

Figure 6

Chart 5.—Relation of various thoracic dimensions to the total body length in well nourished and undernourished infants under 1 year.

Chart 6.—Relation of various abdominal dimensions to the total body length in well nourished and undernourished infants under 1 year.

in relation to the total body length; the thoracic width is relatively larger.

The abdominal area grows at about the same rate in the infants of both groups. The width grows more slowly and the length more rapidly in the undernourished than in the well nourished infant. In relation to the total body length the area and length are relatively larger, while the width shows no significant difference.

The observations of Stewart [3] are of interest in this connection. He underfed rats from birth to 10 weeks of age, with a resulting marked

Comparison of Various Dimensions in Normal and Undernourished Infants

Total Body Length, Range, Mm.	Normal Infants Mean (M_1) and Probable Error, Mm.	Undernourished Infants Mean (M_2) and Probable Error, Mm.	$M_1 - M_2$ and Probable Error, Mm.	$\frac{M_1 - M_2}{\text{Probable Error}}$ and Difference
Transverse Diameter of Heart				
500 to 549	58.2 ± 0.82	53.1 ± 0.58	5.1 ± 1.00	5.1
550 to 599	58.0 ± 0.60	55.7 ± 0.46	2.3 ± 0.75	3.1
600 to 649	64.0 ± 0.69	62.9 ± 0.59	1.1 ± 0.91	1.2
650 to 699	69.1 ± 0.59	64.5 ± 0.69	4.6 ± 0.91	5.1
700 to 749	73.0 ± 0.64	70.2 ± 1.04	2.8 ± 1.22	2.3
Long Diameter of Heart				
500 to 549	63.3 ± 0.89	56.2 ± 0.62	7.1 ± 1.08	6.6
550 to 599	63.0 ± 0.71	59.3 ± 0.48	3.7 ± 8.05	4.4
600 to 649	70.5 ± 0.81	67.3 ± 0.60	3.2 ± 1.01	3.2
650 to 699	74.9 ± 0.67	67.6 ± 0.71	7.3 ± 0.97	7.5
700 to 749	80.2 ± 0.81	75.1 ± 1.05	5.1 ± 1.33	3.8
Diameter of Mediastinum				
500 to 549	31.2 ± 0.53	26.6 ± 0.50	4.6 ± 0.73	6.3
550 to 599	31.0 ± 0.61	26.1 ± 0.47	4.9 ± 0.77	6.4
600 to 649	34.0 ± 0.68	27.5 ± 0.47	6.5 ± 0.82	7.9
650 to 699	31.5 ± 0.54	27.9 ± 0.54	3.6 ± 0.76	4.7
700 to 749	31.6 ± 0.60	31.4 ± 0.99	0.2 ± 1.16	0.2

retardation of growth in body weight. In relation to body weight the stomach and intestines of the underfed animals weighed twice as much as those of normally fed animals of the same body weight.

SUMMARY

The dimensions of the cardiac silhouette and the thoraco-abdominal cavity were measured in a group of undernourished infants, and the averages compared with those of healthy infants by certain subdivisions of age under 1 year.

Retardation of growth during infancy results in a change in the size and relation of the internal organs, as well as in the external dimensions. For the same height, the malnourished infant has a smaller heart and thoracic cavity, a narrower mediastinum and a larger abdominal cavity than the well nourished infant.

3. Stewart, C. A.: Changes in the Relative Weights of the Various Parts, Systems and Organs of Young Albino Rats Underfed for Various Periods, J. Exper. Zoöl. **25**:301, 1918.

BODY BUILD IN INFANTS

VIII. INFLUENCE OF RETARDED GROWTH ON THE DIMENSIONS OF THE ULNA AND THE RADIUS

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AND
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That a reduction in the amount of soft tissues results from undernutrition is well known. The bony skeleton, however, is often looked on as being relatively fixed hereditarily; indeed, the body proportions are widely used by the anthropologist as an index of racial origin. That this concept is erroneous was shown in 1912 by Boas,[1] who demonstrated a change in the cephalic index of the offspring of immigrants to America. More recently it was shown that undernutrition in infants results in a change in the proportions of the external dimensions (measured from bony points), undernourished infants becoming more "linear" than well nourished infants of the same racial origin and from the same social environment.[2]

In the present study the influence of undernutrition on the configuration, relations and texture of the ulna and radius was studied. The infants used in this study have been described in the two preceding papers.[3]

TECHNIC

Roentgenograms were taken with the forearm supinated and the dorsum of the forearm and hand flat against the plate at a distance of 90 cm. Roentgenograms

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From the Department of Diseases of Children, New York University and Bellevue Hospital Medical College, and the Children's Medical Service, Bellevue Hospital.

1. Boas, F.: Changes in Bodily Form of Descendants of Immigrants, New York, Columbia University Press, 1912.

2. Bakwin, H., and Bakwin, R. M.: Body Build in Infants: II. The Proportions of the External Dimensions of the Healthy Infant During the First Year of Life, J. Clin. Investigation **10**:377, 1931. Bakwin, H.; Bakwin, R. M., and Milgram, L.: Body Build in Infants: IV. The Influence of Retarded Growth, Am. J. Dis. Child. **48**:1030 (Nov.) 1934.

3. Bakwin, H., and Bakwin, R. M.: Body Build in Infants: VI. Growth of the Cardiac Silhouette and the Thoraco-Abdominal Cavity, ibid., this issue, page 861. Body Build in Infants: VII. The Effect of Retarded Growth on the Dimensions of the Cardiac Silhouette and the Thoraco-Abdominal Cavity, ibid., this issue, page 870.

were considered unsatisfactory unless the bones appeared as shown in figure 1. The amount of distortion resulting from lack of parallelism of the roentgenograms is small, amounting to about 2 per cent.[4]

Dr. Paul T. Meyers took the roentgenograms used in this study.

The length of the ulna was measured from the proximal margin to the distal margin, parallel to the long axis of the bone.

The diameter of the ulnar diaphysis was measured at about the junction of the middle and the lower third, perpendicular to the long axis of the bone.

The diameter of the ulnar metaphysis was measured on the distal metaphysis of the ulna.

The length of the radius was measured from the proximal margin to the distal margin, parallel to the long axis of the bone.

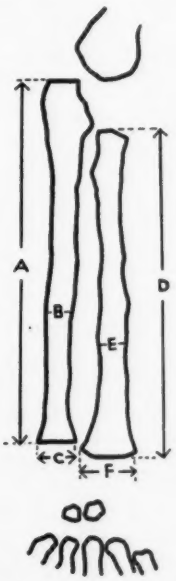

Fig. 1.—Ulna and radius of an infant, showing the dimensions measured: *A* shows the length of the ulna; *B*, the diameter of the ulnar diaphysis; *C*, the diameter of the ulnar metaphysis; *D*, the length of the radius; *E*, the diameter of the radial diaphysis, and *F*, the diameter of the radial metaphysis.

The diameter of the radial diaphysis was measured at about the junction of the middle and the lower third, perpendicular to the long axis of the bone.

The diameter of the radial diaphysis was measured on the distal metaphysis of the radius.

OBSERVATIONS ON MEASUREMENTS

The means and standard deviations for the various dimensions of the ulna and radius in normal infants, by certain subdivisions of age under 1 year, are shown in the table. Because of the relatively small number of cases (266 normal and 224 undernourished infants), the

4. Ritt, E. F., and Sawtell, R. O.: Growth Studies by Roentgen Ray, Am. J. Phys. Anthrop. **14**:1, 1930.

Growth of the Ulna and Radius in Normal Infants by Certain Subdivisions of Age Under 1 Year

Age, Weeks	Number of Cases	Ulna						Radius					
		Length		Diameter of Diaphysis		Diameter of Metaphysis		Length		Diameter of Diaphysis		Diameter of Metaphysis	
		Mean, Mm.	Standard Deviation, Mm.	Mean, Mm.	Standard Deviation, Mm.	Mean, Mm.	Standard Deviation, Mm.	Mean, Mm.	Standard Deviation, Mm.	Mean, Mm.	Standard Deviation, Mm.	Mean, Mm.	Standard Deviation, Mm.
0 to 3	43	63.38	2.81	4.57	0.46	7.42	0.58	55.29	2.83	4.60	0.48	10.44	0.70
4 to 7	33	67.80	2.96	4.84	0.54	7.71	0.74	59.40	3.00	5.14	0.47	11.24	0.90
8 to 15	59	71.61	4.28	5.17	0.71	8.38	0.80	63.09	3.97	5.50	0.63	12.20	1.07
16 to 23	37	75.47	3.57	5.30	0.54	8.79	0.77	67.00	3.86	5.81	0.66	12.81	0.83
24 to 31	24	80.50	4.58	5.70	0.84	9.49	0.79	71.92	4.15	6.48	0.61	13.66	1.17
32 to 39	28	84.77	4.23	5.95	0.98	9.90	1.02	75.63	3.71	6.61	0.55	14.51	1.30
40 to 47	20	90.00	6.95	6.19	0.98	10.29	0.68	81.80	4.60	7.10	0.57	15.18	0.92
48 to 55	22	92.32	4.27	6.28	0.73	10.73	0.93	82.45	3.89	6.88	0.83	15.50	1.38

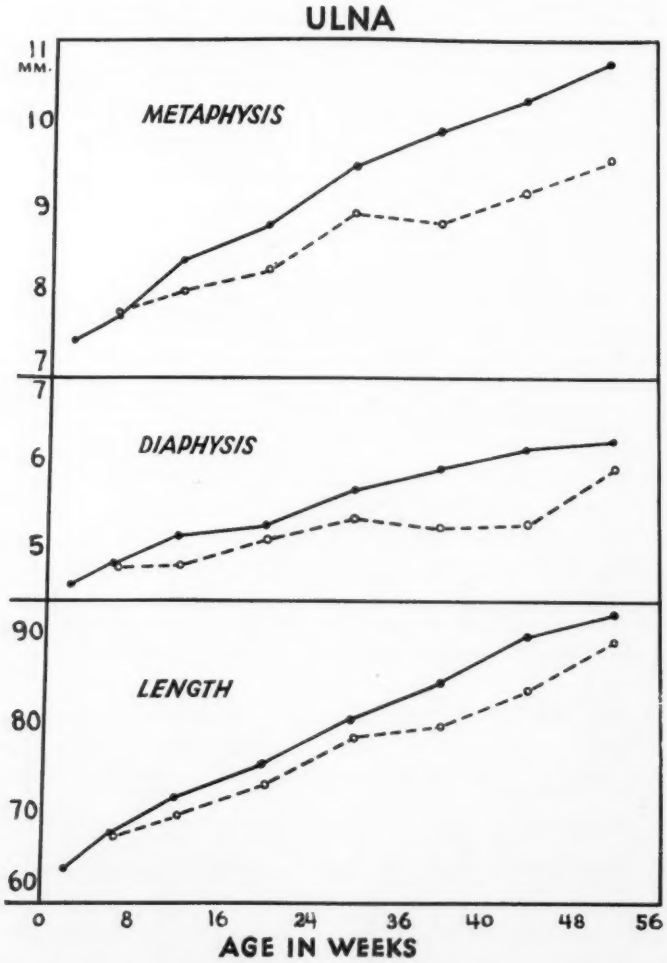

Fig. 2.—Growth of various dimensions of the ulna in normal and undernourished infants. In this figure and in figures 3, 4 and 5 the continuous line indicates the curve for the normal infants, the broken line that for the undernourished infants.

data for both sexes are presented together. The averages for the boys are regularly larger than those for the girls.

The growth curves for the ulna and radius rise gradually (figs. 2 and 3). There is no sharp increase in size during the early weeks of

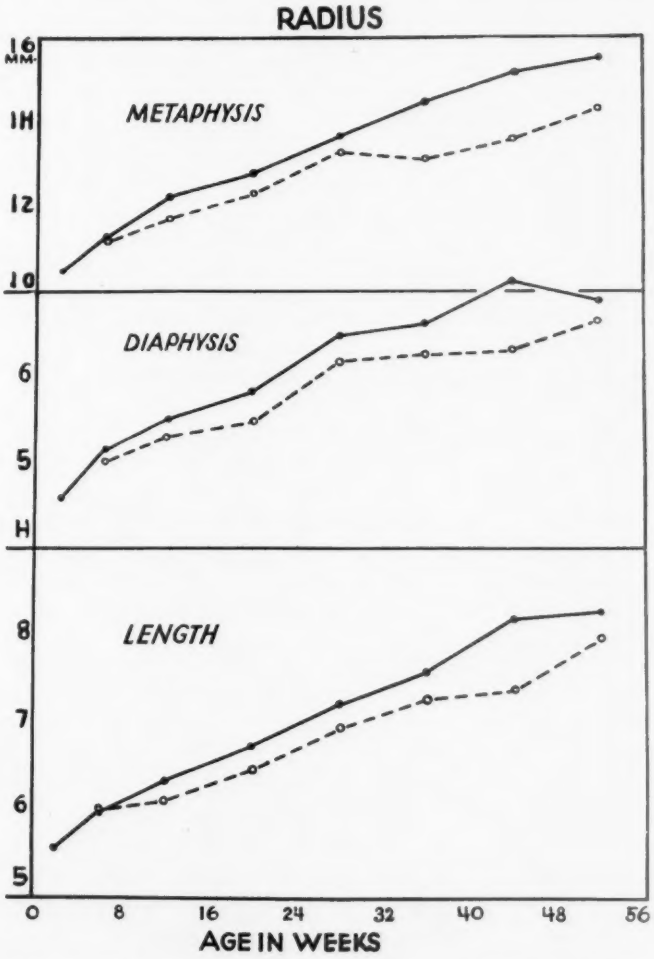

Fig. 3.—Growth of various dimensions of the radius in normal and undernourished infants.

life, as is seen in the curves for most of the external body dimensions.

The growth of the ulna and radius of undernourished infants, illustrated in figures 2 and 3 in relation to that in normal infants, is retarded. The relation of various dimensions of the ulna to the total body length is shown in figure 4. There is no significant difference between the

groups in the relation of the ulnar length to the total body length. The width, however, is regularly relatively narrower in the undernouished than in the normal infants. No definite changes in the proportions of the radius were found. In figure 5 various bony indexes of the ulna

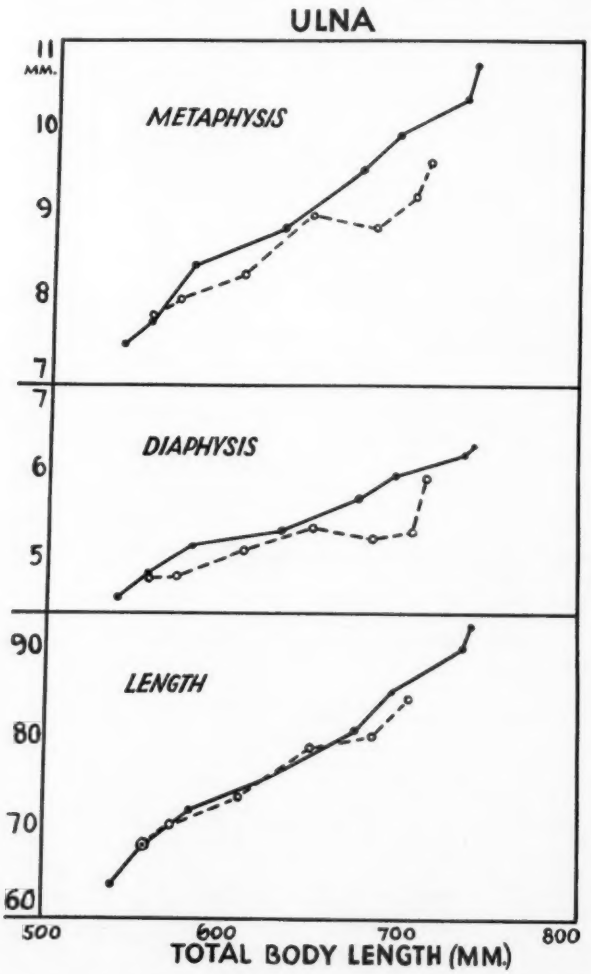

Fig. 4.—Relation of various dimensions of the ulna to the total body length in normal and undernourished infants.

and radius in normal and undernourished infants are compared. The ulna, in both the diaphyseal and the metaphyseal diameters, is consistently broader in the normal than in the undernourished infants. The results of measurement of the radius are not so consistent, but indicate a similar relationship.

Bony Texture.—In severely malnourished infants there are striking changes in the appearance of the bones. The cortex is thin and dense; the bony outlines are sharply demarcated; the trabeculation is fine, and the bone is more transparent than normal. The bones of the leg of an infant 14 months old weighing 4,800 Gm. are shown in figure 6.

Ossification of Carpal Centers.—During the first month of life about 20 per cent of infants showed ossification of one or more carpal centers.

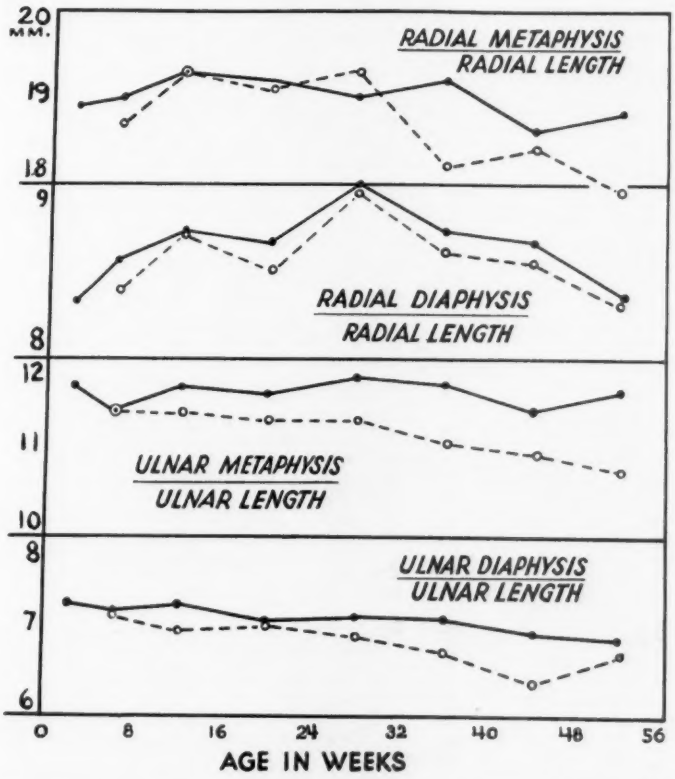

Fig. 5.—Comparison of various bony indexes in normal and undernourished infants by certain subdivisions of age under 1 year.

Hess and Weinstock [5] found that about 10 per cent of the white boys born at full term and about 20 per cent of the white girls born at full term show carpal ossification within the first twelve days of life. The percentage rises rapidly, and after the thirty-first week of life only

5. Hess, A. F., and Weinstock, M.: A Comparison of the Evolution of Carpal Centers in White and Negro New-Born Infants, Am. J. Dis. Child. **29**:347 (March) 1925.

occasional infants fail to show ossified carpal centers. The rate is slightly accelerated in the girls, as was noted by Pryor.[6] No difference was found in the rate of ossification of the carpal centers in the normal and undernourished infants.

Fig. 6.—Bones of the leg of an infant 14 months old weighing 4.8 Kg. The cortex is thin and sharply defined, and the bones are more transparent than in a normal child.

6. Pryor, J. W.: The Ossification of the Epiphyses of the Hand, Bull. State Coll. Kentucky, October 1906, ser. 3, no. 4. The Chronology and Order of Ossification of the Bones of the Human Carpus, Bull. State Univ., Lexington, Kentucky, April 1908, new ser. 1, no. 2.

In the rats which Jackson [7] kept at their weight at birth for a period of twelve days after birth by underfeeding, ossification of centers occurred, but at a slower rate than was observed in normally fed rats of the same age.

SUMMARY

The dimensions of the ulna and radius of normal and undernourished infants were compared.

It was shown that the ulna and radius of undernourished infants grow more slowly in all dimensions than those of normal infants.

The bones of the undernourished infants were narrowed in relation to the length of the bones and to the total body length than those of the normal infants.

There was no difference between the two groups in the rate of ossification of the carpal centers.

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7. Jackson, C. M.: Structural Changes When Growth Is Suppressed by Undernourishment in the Albino Rat, Am. J. Anat. **51**:347, 1932.

STUDIES ON LIPOIDS AND LIPOID DISEASES

IV. THE LIPOID CONTENT OF TISSUES IN CASES OF STATUS EPILEPTICUS, TOXIC ENCEPHALOPATHY AND CHRONIC LEPTOMENINGITIS

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The beneficial effects of the ketogenic diet high in fats in a goodly percentage of the cases of marked epilepsy in children treated by this means prompted McQuarrie, Husted and Bloor [1] to investigate the lipoids of the blood plasma in epilepsy. Prior to this work, observations had been made on the cholesterol content of the blood in epilepsy, but no uniformity of results was established. Some investigators found hypocholesteremia, and some, hypercholesteremia, while others were unable to demonstrate any change in the cholesterol content of the blood. Until the report of McQuarrie and his associates, little or no knowledge was obtainable concerning the other blood lipoids in epilepsy. These workers demonstrated clearly that the phospholipoid-cholesterol ratio in the blood of an epileptic patient during, or just preceding or following, an attack is higher than at any other time, thus establishing definitely a relationship of the blood lipoids to status epilepticus. This relationship obtains whether the cholesterol content of the blood is high or low.

This information was of interest to us since we had had an opportunity in August 1932 to determine the lipoid content of some of the tissues of an epileptic child dying in status epilepticus. A higher phospholipoid-cholesterol ratio was found in the tissues of this child than in those of a child with Schüller-Christian's disease and of one with severe anemia [2] whose cases were previously reported. Since we were unable to find in the literature any records of analysis of the tissues of children and since the two children whose cases we had reported were

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From the Departments of Pediatrics and Infectious Diseases, University of Michigan Medical School.

1. McQuarrie, I.; Husted, C., and Bloor, W. R.: Lipids of Blood Plasma in Epilepsy; Variation of Lipids in Relation to Occurrence of Seizures, J. Clin. Investigation **12**:255, 1933.

2. Cowie, D. M., and Magee, M. C.: Lipoids and Lipoid Diseases: III. Lipoid Content of Tissues in Schüller-Christian's Disease (Xanthomatosis) and Review of Literature on Lipoid Content of Human Tissues, Arch. Int. Med. **53**:391 (March) 1934.

much younger (2 years and 10 months, respectively) than the epileptic child (8 years), we thought it advisable to determine the lipoid content of the tissues of children of approximately the same age dying of other causes. One of these children was a patient with toxic encephalopathy with a history of an acute illness of five days during the last three of which marked muscular twitchings were a prominent manifestation. The other child, a patient with chronic leptomeningitis, without convulsions, who was acutely ill for only five days, died of respiratory and circulatory complications. The cases of these three patients are of interest for comparison, since in each the central nervous system was involved. We are also recording the lipoid content of the lungs and skeletal muscle of a child dying of lymphatic leukemia.

CASE 1.—*Epilepsy.*

I. F., a colored boy, 8 years old, was determined to have idiopathic epilepsy in May 1930. The manifestations appeared two months prior to examination. Attacks of grand mal recurred every other day. The physical examination showed a well developed boy and revealed nothing abnormal. A month later the attacks became more pronounced. A ketogenic diet while in the hospital seemed beneficial, but phenobarbital was a necessary adjunct. The diet could not be carried out in the child's home. He was again seen in the clinic in January 1932. Attacks had been recurring more frequently. In April a tonsillectomy was done. In August the attacks occurred every two hours for seven days. The examination of the fundi and the Kahn test of the blood gave negative results. A lumbar puncture showed the fluid to be under increased pressure; there were 2 cells per cubic centimeter; the sugar content was 80 mg. per hundred cubic centimeters; the chlorides, 680 mg. per hundred cubic centimeters; the colloidal gold, mastic and Kahn tests of the spinal fluid gave negative results; globulin was present as a trace. On August 8 there were several attacks during the day. On the night of August 9 and of August 10 the attacks of grand mal were preceded by maniacal symptoms. The patient became very noisy, attempted to jump out of bed and had visual hallucinations. Roentgen examination of the skull gave negative results. The blood count was as follows: red cells, 5,640,000; white cells, 11,440; hemoglobin, 82 per cent (Sahli); polymorphonuclears, 70 per cent; lymphocytes, 20 per cent; eosinophils, 5 per cent; monocytes, 5 per cent; platelets, normal. Urinalysis gave negative results.

On August 11, at 7 a. m., the temperature was 105.8 F., the pulse rate, 144 and the respiratory rate, 48. Attacks of grand mal occurred almost continuously. The clinical diagnosis was bronchopneumonia. An oxygen tent was used. Two grains (0.129 Gm.) of phenobarbital sodium was given hypodermically.

On August 12, at 3:45 a. m., the convulsions had become infrequent since the child was placed in the oxygen tent. The temperature was 106.2 F. and the respirations, 60; the patient was semistuporous. At 11:30 p. m. the temperature was 106.6 F., and the respiratory rate, 52; the child was comatose; the results of examination of the lungs and heart were negative. The extremities were cold. The pupils were dilated and did not react to light. In the morning 500 cc. of a solution of dextrose was given intravenously; in the evening, 50 cc.

On August 13, at 4:45 a. m., the patient died. A record of the number of epileptic seizures is recorded in table 1.

The pathologic diagnosis at autopsy was: acute purulent bronchitis and confluent purulent lobular pneumonia; status epilepticus; intense acute passive congestion of all the organs; petechial hemorrhages in the meninges and lungs; a patch of pulmonary atelectasis and emphysema; dehydration; slight parenchymatous degeneration of all the organs, and pyorrhea alveolaris.

The brain was of normal size and consistency. The convolutions were normally developed. The leptomeninges were smooth. The gray matter of the frontal sections was of normal width and distinctly hyperemic; the white matter appeared normal. The basal ganglions presented an appearance similar to that of the gray matter. The ventricles were narrow with smooth ependyma. The aqueduct was not enlarged. The pons medulla and cerebellum were moderately hyperemic. The basal vessels were delicate; the gray matter was moderately hyperemic. There was passive congestion of the pituitary gland, and eosinophils were present in excess.

CASE 2.—*Toxic encephalopathy.*

S. L., a white boy, 10 years old, was brought to the clinic on March 3, 1933, because he failed to recognize people and objects. There was a history of possible

TABLE 1.—*Clinical Data in a Case of Status Epilepticus*

August 1932	Highest Temperature, F.	Highest Pulse Rate	Highest Respiratory Rate	Number of Epileptic Seizures
8	100	95	22	5
9	100.5	110	22	21; at 9:45 p. m., maniacal symptoms developed
10	101	130	25	24
11	105	165	63	53; continuous from 8 to 12 a. m.
12	106.5	170	60	None since midnight; died at 4 p. m.

exposure to tuberculosis two years prior to admission. Two days before entrance to the clinic he carried a toy airplane to school, which the teacher took away from him. He returned home in a much agitated state and refused to eat. That night he talked in his sleep more than usual. The next day he vomited many times, became disoriented and recognized his parents only occasionally. The gait was unsteady. He was delirious at night. He had not recognized his parents since that time. No history of accidents or infections could be obtained.

Physical examination showed the patient to be acutely ill and delirious. The temperature was 103 F. and later 104 F. The eyes were staring, and the head was held to the left. The child did not speak. There were occasional small twitchings of the mouth; the pupils were dilated and reacted slightly to light; there was no nystagmus; the teeth were clenched. The results of examination of the lungs, heart, abdomen and genitals were negative. Intermittent rigidity (spasticity) of the extremities was marked. There were slow athetoid movements at times. The toes were held in marked dorsal flexion. There was flexion of the knees on plantar irritation. No ankle clonus was elicited. The deep reflexes were markedly hyperactive. The cremasteric reflex was obtained. The superficial abdominal reflexes were not present; there was an intermittent Brudzinski sign but no Kernig sign. The eyegrounds were hyperemic.

Examination of the blood showed: red cells, 5,560,000; white cells, 27,600; polymorphonuclears, 62 per cent; lymphocytes, 22 per cent; monocytes, 0, and eosinophils, 2 per cent. The spinal fluid was under a pressure of from 150 to 160 mm. of mercury and was clear; the Pandy test gave a reaction of +++; the

cell count was 30; the colloidal gold curve, 0013321000; the reaction for globulin, ++++; the sugar content, from 100 to 187 mg. per hundred cubic centimeters, and the sodium chloride content, 660 mg. per hundred cubic centimeters. The carbon dioxide content of the blood was 49 volumes per cent; the nonprotein nitrogen, 50 mg. per hundred cubic centimeters, and the calcium, 11 mg. per hundred cubic centimeters. The Kahn test was negative.

On March 3, there was rigidity of the neck, the right arm and the right leg, and involuntary twitching was present in all the extremities, but more in the left arm and leg. There was involuntary urination. Moderate cyanosis was noted. The pulse and respirations were rapid and irregular. The use of a restraining jacket was necessary because of the extreme restlessness. At 12 noon, 75 cc. of a 35 per cent solution of dextrose was given intravenously; 10 units of insulin and 1,000 cc. of Ringer's solution were also administered. The temperature reached 109.8 F.

On March 4 at 3 a. m., 75 cc. of a 35 per cent solution of dextrose was given intravenously. At 9 a. m. the temperature was 103 F.; at 6 p. m. there was twitching of the face and arms. At 7 p. m., 75 cc. of a 35 per cent solution of dextrose was given intravenously. Ten units of insulin and 1,000 cc. of Ringer's solution were administered.

On March 5 at 3:30 a. m. the patient became worse, and at 10:30 a. m. he died.

The pathologic diagnosis at autopsy was: acute purulent bronchitis and bronchopneumonia; pulmonary congestion; edema; emphysema and multiple hemorrhages (phenobarbital); toxic encephalopathy (?)—multiple petechial hemorrhages in the substance of the brain, marked cerebral congestion and edema and moderate thickening of the leptomeninges; thymicolymphatic constitution; marked congestion of all the organs.

CASE 3.—*Chronic leptomeningitis; internal hydrocephalus.*

S. S., a girl of 8 years, entered the clinic on March 11, 1933, because of vomiting, headache, pain in the head and neck, deep sighing, attacks of air hunger, and "fainting spells," from which she could not be aroused.

On March 8, there was marked rigidity of the neck and a positive Kernig sign. The spinal fluid was under marked pressure and was clear; the cell count was 2; there were traces of globulin and of sugar. The Wassermann and Kahn tests were negative. Examination of the fundi revealed choked disks, tortuous vessels, marked edema and a few hemorrhages. The blood count was: red cells, 4,600,000; white cells, 10,600; hemoglobin, 95 per cent (Sahli); polymorphonuclears, 82 per cent, and lymphocytes, 18 per cent. The temperature ranged from 97 to 100 F.; the pulse rate, from 106 to 120.

On admission the patient was lethargic. The speech was sluggish; she was dehydrated and slightly disoriented. There was marked mucous secretion in the throat and nasal passages. Lateral rotation of the eyes was impossible. By a right ventricular puncture, 100 cc. of fluid was removed under a pressure of 400 mm.; the cell count was 2. At 9 p. m. dextrose was given intravenously; at 10:45 p. m. the respirations became labored and cyanosis developed. At 11:20 p. m. a ventricular puncture revealed markedly increased pressure of the spinal fluid. Forty cc. of a 50 per cent solution of dextrose was given intravenously. At 12:10 a. m., with the patient under avertin anesthesia, a suboccipital decompression was done. No tumor was found. The fluid reformed rapidly. The respirations became labored, and the patient died on the following day.

The pathologic diagnosis was: exploratory craniotomy; localized chronic leptomeningitis with adhesions; dilatation of the ventricles; prolonged increased intracranial pressure; pulmonary edema and congestion; patchy pulmonary atelectasis;

slight endocardial sclerosis of the cusps of the mitral valves; fatty infiltration of the liver; passive congestion of all the organs; productive pachymeningitis; multiple hemorrhagic necroses in the brain; thymicolymphatic constitution; a small ulcer in the duodenum; marked congestion and parenchymatous degeneration of all the organs; degenerative fatty infiltration of the liver.

The microscopic diagnosis was: congestion of the substance of the cord and the meninges; slight dilatation of the central canal; marked congestion of the cortex with a small area of recent hemorrhage and perivascular edema; recent hemorrhages near the surface of the cerebellum with an area of anemic necrosis near an area of hemorrhage; slight perivascular infiltration; well marked thickening of the dura mater; a normal pineal body; marked congestion of the pituitary gland with eosinophils in excess; congestion and edema of the leptomeninges; old thickening with more recent inflammatory infiltrations.

CASE 4.—*Acute lymphatic leukemia.*

W. M., a white girl, 12 years old, was taken ill in September 1932, with a cold in the head and painful swellings behind the ears. Pain in the joints recurred about every other day. In December there was marked epigastric pain. The patient became "very nervous"; the muscles were sore at various places. There was marked sweating at night. Recently, there had been dyspnea, and for a few days prior to admission a fine rash had appeared over the ankles. The patient entered the hospital on Jan. 25, 1933. The temperature was 100.6 F. The spleen extended two fingerbreadths to the left of the navel; the liver, two fingerbreadths below the ribs. The submaxillary glands were enlarged and slightly tender. The cervical and inguinal glands were palpable but not remarkable. The blood count revealed: red cells, 1,970,000; white cells, 52,000; hemoglobin, 34 per cent (Sahli). Most of the cells were large and immature lymphocytes. The platelets were reduced. Nucleated red cells were found. The clinical diagnosis was acute or subacute lymphatic leukemia. The patient died soon after entering the hospital.

The pathologic diagnosis at autopsy was: leukemic lymphoblastoma; lymphoblastomatous transformation of the lymph nodes, bone marrow, thymus and spleen with lymphoblastic infiltration of the gastro-intestinal tract, pancreas, liver, kidneys, retroperitoneal tissues, dura mater, myocardium, ovaries and uterus; terminal dilatation of the right side of the heart with relative tricuspid and pulmonary insufficiency; bronchial asthma; thymicolymphatic constitution (persistent hyperplastic thymus, generalized lymphoid hyperplasia and hypoplasia of the suprarenals); petechial hemorrhages in the skin; passive congestion; slight parenchymatous degeneration of all the organs.

ANALYSES OF TISSUES

In table 2 are recorded the results of the analyses of the tissues for total lipoid,[3] phospholipoid[4] and cholesterol[5] in the four cases. The phospholipoid-cholesterol ratio is indicated. The results of the analyses of the various tissues in two cases previously reported are also tabulated, as well as those of the analyses of voluntary muscle by Jewett (1931).[6] The report by this worker is the only reference we have been able to

3. Prolonged extraction by alcohol and ether; gravimetric method.[2]
4. Whitehorn's method for lipoid phosphorus; factor 26.[2]
5. Sackett's method.
6. Jewett, M.: Biochem. J. **25**:1991, 1931.

find which gives the analyses both of phospholipoid and of cholesterol in human tissues. Unfortunately, we were able to secure tissue from only the liver, spleen, lungs and voluntary muscle in the case of epilepsy. In all of these tissues, with the exception of that of the lungs, it will be seen that the phospholipoid-cholesterol ratio is much higher than in similar tissues of children dying of other causes. The higher ratio is even more marked than that reported by McQuarrie, Bloor and Husted in the blood of epileptic patients.

Liver.—The variation in the total lipoid of the liver was marked. In the three cases in which the tissues showed fatty infiltration, there was a much higher lipoid content than in the two in which the tissues showed no such pathologic condition. The phospholipoid content varied from 1.79 to 3.12 Gm. per hundred grams of fresh tissue. It apparently had no relation to the fatty infiltration and was highest in the case of status epilepticus. The cholesterol content varied from 0.273 to 0.398 Gm. and was lowest in the cases of epilepsy and anemia. The phospholipoid-cholesterol ratio in the case of status epilepticus was 11.4 : 1, while the ratios in the other cases varied from 5 : 1 to 6.5 : 1.

Spleen.—The total lipoid content of the spleen was lower than that of the liver, varying from 2.36 to 4.25 Gm. In the spleen as in the liver the phospholipoid content was highest in the case of epilepsy, in which the lowest cholesterol content was found to be 0.153 Gm. There was a marked variation in the cholesterol content of the spleens, from 0.1532 to 0.597 Gm. Here again the phospholipoid-cholesterol ratio in the case of epilepsy was much higher, 13.2 : 1. The ratio in the other cases varied from 2.8 : 1 to 5.3 : 1.

Lungs.—In the lungs there was no appreciable difference between the phospholipoid-cholesterol ratio in the case of epilepsy and that in the other cases. The range of the phospholipoid content of the lungs in the various cases was from 1.2 to 2.26 Gm., the highest values being found in the case of lymphatic leukemia. We are unable to say whether this finding is of significance, but it is of interest that the cholesterol content of the lungs in this case was the highest of those analyzed (0.444 Gm.). It was even higher than that of the lungs in the case of Schüller-Christian's disease, which showed fat-containing phagocytes in the alveoli and in the perivascular tissues. The cholesterol content of the lungs of the epileptic patient was low, only 0.242 Gm.

Kidneys.—The phospholipoid and cholesterol content of the kidneys, as well as the phospholipoid-cholesterol ratio, shows a range similar to that found in the lungs. No observations were made in the case of epilepsy.

Voluntary Muscle.—The voluntary muscle showed the lowest content of phospholipoids of any of the tissues examined. In nine specimens

TABLE 2.—*Lipoids in Various Tissues in Cases of Status Epilepticus, Acute Encephalopathy, Chronic Leptomeningitis, Schüller-Christian's Disease and Severe Anemia*

Tissue	Age	Sex	Clinical Diagnosis	Pathologic Diagnosis of Tissue	Total Lipoid, Gm. per 100 Gm. Fresh Tissue	Phospho-lipoid, Gm. per 100 Gm. Fresh Tissue	Choles-terol, Gm. per 100 Gm. Fresh Tissue	Phospholipoid-Cholesterol Ratio	Investigator
Liver.....	10 mos.	F	Anemia	Cloudy swelling; fatty infiltration	8.09	1.79	0.280	6.4 : 1	Cowie and Magee, 1933
	2 yrs.	F	Schüller-Christian's disease	Atrophy; increased stroma	3.17	2.24	0.398	5.6 : 1	Cowie and Magee, 1933
	10 yrs.	M	Acute encephalopathy	Cloudy swelling; congestion; small hemorrhages on surface	4.06	2.52	0.389	6.5 : 1	
	7 yrs.	F	Chronic leptomeningitis	Congestion; cloudy swelling; degenerative fatty infiltration	9.18	1.799	0.357	5 : 1	
	8 yrs.	M	Status lymphaticus	Congestion; cloudy swelling; diffuse degenerative fatty infiltration	7.10	3.12	0.273	11.4 : 1	
Lung.....	10 mos.	F	Anemia	Aspiration pneumonia; lower lobe used in analysis and showed least involvement	4.62	1.33	0.335	4 : 1	Cowie and Magee, 1933
	2 yrs.	F	Schüller-Christian's disease	Perivascular, peribronchial fibrosis; phagocytes containing fat in these areas and in the alveoli	3.01	1.68	0.432	3.9 : 1	Cowie and Magee, 1933
	10 yrs.	M	Acute encephalopathy	Congestion; emphysema; small hemorrhages; acute bronchopneumonia; acute edema	3.05	1.20	0.360	3.3 : 1	
	7 yrs.	F	Chronic leptomeningitis	Congestion; emphysema; early lobular pneumonia; patchy atelectasis	3.15	1.495	0.426	3.5 : 1	
	13 yrs.	F	Lymphatic leukemia	Slight lymphoblastomatous infiltration around the bronchi; bronchial asthma	4.38	2.26	0.444	5.1 : 1	
	8 yrs.	M	Status epilepticus	Patchy atelectasis; emphysema; acute purulent bronchitis and bronchopneumonia; passive congestion	3.412	1.51	0.242	6.2 : 1	

Spleen.....	10 mos.	F	Anemia	Congestion	3.64	1.43	0.337	4.2 : 1	Cowie and Magee, 1933
	2 yrs.	F	Schüller-Christian's disease	Congestion; localized areas of fibrous tissue containing foam cells and phagocytes	2.36	1.53	0.286	5.3 : 1	Cowie and Magee, 1933
	10 yrs.	M	Acute encephalopathy	Passive congestion	2.61	1.14	0.401	2.8 : 1	
	7 yrs.	F	Chronic leptomeningitis	Chronic passive congestion; lymphoid hyperplasia	4.25	1.716	0.597	2.9 : 1	
	8 yrs.	M	Status epilepticus	Passive congestion; lymphoid hyperplasia	2.68	2.02	0.153	13.2 : 1	
Kidney.....	10 mos.	F	Anemia	Passive congestion; cloudy swelling	4.02	1.14	0.362	3.1 : 1	Cowie and Magee, 1933
	2 yrs.	F	Schüller-Christian's disease	Cloudy swelling; calcification of renal vessels; calcium in tubules	2.40	1.33	0.250	5.3 : 1	Cowie and Magee, 1933
	10 yrs.	M	Acute encephalopathy	Cloudy swelling; passive congestion	3.65	1.58	0.345	4.6 : 1	
	7 yrs.	F	Chronic leptomeningitis	Congestion; cloudy swelling; slight degenerative fatty infiltration	4.70	1.526	0.366	4.2 : 1	
Heart muscle..	10 mos.	F	Anemia	Hypoplasia	4.19	1.43	0.118	12.1 : 1	Cowie and Magee, 1933
Left ventricular wall	2 yrs.	F	Schüller-Christian's disease	Subendocardial degenerative fatty infiltration	2.66	1.82	0.174	10.5 : 1	Cowie and Magee, 1933
	10 yrs.	M	Acute encephalopathy	Hypoplasia; passive congestion	4.25	1.93	0.281	6.9 : 1	
	7 yrs.	M	Chronic leptomeningitis	Hypoplasia; cloudy swelling	3.63	1.583	0.212	7.4 : 1	
Voluntary muscle									
Pectoralis....	?	?	Normal	.....	8.74	0.667	0.351	1.9 : 1	Jewett, 1931 [6]
Pectoralis....	?	?	Normal	.....	7.28	0.530	0.377	1.4 : 1	Jewett, 1931 [6]
Rectus.....	10 mos.	F	Anemia	Congestion	5.9	0.49	0.121	4 : 1	Cowie and Magee, 1933
Rectus.....	2 yrs.	F	Schüller-Christian's disease	Edematous; pale	0.9	0.47	0.128	3.7 : 1	Cowie and Magee, 1933
Psoas.....	2 yrs.	F	Schüller-Christian's disease	Edematous; pale	0.84	0.47	0.110	4.3 : 1	Cowie and Magee, 1933
Psoas.....	10 yrs.	M	Acute encephalopathy	Normal	3.00	0.89	0.152	5.8 : 1	
Psoas.....	7 yrs.	F	Chronic leptomeningitis	Normal	2.74	0.886	0.189	4.7 : 1	
Psoas.....	13 yrs.	F	Lymphatic leukemia	Normal	3.21	0.624	0.164	3.8 : 1	
Psoas.....	8 yrs.	M	Status epilepticus	Normal	2.53	0.78	0.046	17.0 : 1	

the content varied from 0.047 to 0.89 Gm. The lowest values were found in the cases of Schüller-Christian's disease and anemia. The cholesterol content of the voluntary muscle was also low. In our own case it varied from 0.046 to 0.189 Gm. The cholesterol content of the muscle in the two cases reported by Jewett was higher (0.351 and 0.377 Gm.). Again the phospholipoid-cholesterol ratio in the muscle in the case of epilepsy was much higher (17 : 1) than that of the muscle in the other cases (from 1.4 : 1 to 5.8 : 1).

Heart Muscle.—A part of the wall of the left ventricle was used in each analysis. Very high phospholipoid-cholesterol ratios were found in the muscle in the cases of Schüller-Christian's disease and anemia. There is a marked difference in the ratio for heart muscle and that for voluntary muscle in the same cases. However, in the cases of acute

TABLE 3.—*Lipoids in Various Tissues in a Case of Status Epilepticus Compared With Those in Cases of Other Conditions*

	Status Epilepticus			Other Conditions				
					Phospholipoid, Gm. per 100 Gm. of Tissue		Cholesterol, Gm. per 100 Gm. of Tissue	
Tissue	Phospholipoid, Gm. per 100 Gm. of Tissue	Cholesterol, Gm. per 100 Gm. of Tissue	Phospholipoid, Cholesterol Ratio	Phospholipoid-Cholesterol Ratio Maximum	Minimum*	Maximum*	Minimum	Maximum
Liver	3.12	0.273	11.4 : 1	6.5 : 1†	1.79	2.52	0.280	0.398
Spleen	2.02	0.153	13.2 : 1	5.3 : 1‡	1.14	1.72	0.286	0.597
Lung	1.51	0.242	6.2 : 1	5.1 : 1‖	1.33	2.26	0.335	0.444
Muscle	0.78	0.046	17.0 : 1	5.8 : 1§	0.47	0.89	0.110	0.189

* Minimum: the lowest phospholipoid content found in any case; maximum: the highest phospholipoid content found in any case.

† Obtained from one case of acute encephalitis (encephalopathy) in a child of 10 years (table 2).

‡ Obtained from one case of Schüller-Christian's disease in a child of 2 years (table 2).

‖ Obtained from one case of lymphatic leukemia in a child of 13 years (table 2).

§ Obtained from one case of chronic leptomeningitis in a child of 12 years (table 2).

encephalitis and chronic leptomeningitis, the difference between the ratios for the heart muscle and the voluntary muscle is not so marked. This increase in the phospholipoid-cholesterol ratio is of interest. No explanation is at hand. There was a great similarity in the lipoid content of the various tissues in the cases investigated. The cholesterol content of the spleen, lungs and voluntary muscle was lowest in the case of epilepsy. The phospholipoid content of the liver and spleen was highest in the case of epilepsy. This is analogous to the findings in the blood plasma of McQuarrie and his co-workers. The phospholipoid content was highest in the lung in the case of leukemia. The point of interest centers around the phospholipoid-cholesterol ratio, which was consistently higher in the liver, spleen, lungs and voluntary muscle of the patient with epilepsy dying during status epilepticus. This is well shown in table 3.

It is of interest in this connection that when normal animals are given cholesterol intravenously narcosis results and that just the opposite results are obtained when lecithin is given in conjunction with a narcotic.[7]

CONCLUSIONS

The total lipoid, cholesterol and phospholipoid contents of the various tissues of an epileptic child dying in status epilepticus, compared with similar observations on patients with other pathologic conditions, are recorded.

In the case of epilepsy during status epilepticus the phospholipoid-cholesterol ratio of the liver, spleen and particularly the various skeletal muscles was markedly higher, and that of the lung definitely higher, than in the other cases which were observed (Schüller-Christian's disease, acute encephalopathy, chronic leptomeningitis and severe anemia).

These observations supplement those of McQuarrie, Husted and Bloor on the blood plasma of epileptic patients. Analogous situations occur in the various tissues in regard to lecithin, cholesterol and the lecithin-cholesterol ratio.

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7. McQuarrie, Husted and Bloor,[1] p. 263.

VIRUS—ANTIVIRUS MIXTURES IN SMALLPOX VACCINATION

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Since the time of Jenner (1791) it has been recognized that the use of a virus attenuated by passage through animals of another species can confer a high degree of immunity. Nevertheless, in the years since then the technical procedure employed in the inoculation of vaccinia virus as a prophylactic measure against the allied, more severe disease smallpox has undergone few essential modifications. The method employed at present for immunization against smallpox is certainly not completely satisfactory. The local reaction is often quite marked and may result in a rather unsightly scar; at times secondary pox appears at distant sites. The frequent concomitant systemic reaction is also of importance, especially in young infants, in whom the high temperature and general malaise often result in a general lowering of resistance and an increased susceptibility to infection of the respiratory and intestinal tracts. The occurrence of erysipelas about the local lesion is also not rarely encountered. Moreover, the occasional appearance of encephalitis after inoculation with vaccinia virus cannot be overlooked; whether due to the vaccinia itself or to some associated virus, the encephalitis appears to bear a close relationship to the lesion produced as a result of the local inoculation of the vaccinia virus.

Methods of producing a degree of immunity to smallpox without the lesions of pustular vaccinia have until recently never proved completely successful. However, recent investigation in the field of virus disease, especially by Andrewes,[1] Rhoads[2] and Findlay and Hindle,[3] have seemed to offer a means toward the desired end. The use for immunization of a pathogenic agent neutralized or rendered innocuous by its association with a specific antisubstance is not new; it was

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1. Andrewes, C. H.: Action of Immune Serum on Vaccinia and Virus III in Vitro, J. Path. & Bact. **31**:671 (Oct.) 1928. Anti-Vaccinial Serum: Protection Against Generalization in Rabbit, ibid. **32**:265 (April) 1929; Anti-Vaccinial Serum: Evidence of Slow Union with Virus in Vitro, ibid. **33**:265 (April) 1930.

2. Rhoads, C. P.: Immunization Against Vaccinia by Non-Infective Mixtures of Virus and Immune Serum, J. Exper. Med. **53**:185 (Feb.) 1931.

3. Findlay, G. M., and Hindle, E.: Combined Use of Living Virus and Immune Serum for Immunization Against Virus Infections, Brit. M. J. **1**:740 (May 2) 1931.

originated by von Behring,[4] in 1913, who demonstrated that it is possible to immunize animals against diphtheria by the use of toxin-antitoxin mixtures. In the field of the viruses, Andrewes contributed the important fact that the vaccinia virus is not destroyed by contact in vitro with its specific antiserum. He showed that the combination of the two is a loose union, and that by filtration through a Berkefeld candle antibodies can be recovered quantitatively from a mixture of immune serum with an excess of virus, even after contact of twenty-four hours; conversely, active vaccinia virus can be recovered from a mixture of virus with an excess of immune serum left in contact for some hours; nevertheless after prolonged contact for a number of days in vitro some stable union of antigen and antibody may occur. Andrewes further showed that vaccinia in an inactive serum-virus mixture can be reactivated by simple dilution of the mixture with Ringer's solution or with normal rabbit serum. When working with a potent testicular strain of neurovaccine, which produced generalized lesions of the skin in 79 per cent of rabbits inoculated intradermally, he prevented this generalization by giving comparatively small doses (3 cc.) of immune serum intravenously at the time of inoculation; the local lesion, however, was unaffected. With the same vaccine, generalized lesions always appeared in the skin of the rabbit given intravenous injections of more than 500 skin-infecting doses; however, by mixing immune serum with the virus or by injecting the serum shortly before the virus was injected the generalization could be prevented. Approximately 1 cc. of serum was necessary for every 1,000 minimum infecting doses (M.I.D.). Fifty per cent of the rabbits in which the serum prevented generalization were found on subsequent tests to have active immunity, as evidenced by the lack of gross evidence of generalized vaccinia; histologic studies were not made.

Rhoads also showed that vaccine virus and specific immune serum, mixed in such proportions as to produce no lesion when inoculated intradermally, could induce immunity when instilled into the nasal cavity of rabbits or inoculated subcutaneously; in the production of this immunity there was no local reaction and only a minimum of systemic reaction. However, Rhoads emphasized the importance of the complete neutralization of the vaccine virus, for unless this occurred generalized vaccinia resulted. In most instances 0.2 cc. of immune serum sufficed to neutralize an equal amount of 1:100 dilution of a virus which gave rise to lesions when inoculated alone in a dilution of 1:100,000. In Rhoads' studies, histologic examination of the nasal mucosa, brain, lungs, spleen, liver and testicles of rabbits treated with properly neutralized material revealed no vaccinal lesions; however, the virus could often be recovered from the nasal mucosa, from the brain

4. von Behring, E.: Deutsche med. Wchnschr. **39**:873, 1913.

and occasionally from the lung. This was in accord with the observation of Demme,[5] which indicated that active virus may be present in the tissues without giving rise to lesions.

EXPERIMENTS

Using the work of Andrewes and of Rhoads as a basis, it was decided to determine what proportion of immune serum, when mixed with vaccine virus, would prevent the occurrence of a local lesion when inoculated intradermally into infants not immune, and whether or not infants so treated would exhibit an immune reaction when subsequently retested with an undiluted potent virus vaccine. In the following experiments the vaccine used was a stock solution of glycerinized virus vaccine supplied by the laboratories of the New York City Department of Health. This was regularly tested to insure the retention of its potency.

Experiment 1.—*Vaccination with Virus Diluted with Varying Proportions of Slightly Immune Serum.*

Blood serum was obtained from two healthy children, each of whom had been successfully vaccinated five years previously. Vaccine virus was then mixed with this serum in definite proportions, the amounts varying from 1 part of vaccine with 1 part of serum to 1 part of vaccine with 20 parts of serum. The mixture of vaccine and serum was then allowed to incubate for one hour at room temperature.

Thirty-nine children varying in age from 6 months to 2 years, none of whom had previously been vaccinated, were then inoculated with the mixture, the following technic being used: One drop of the mixture was placed on the previously cleansed dry skin of the upper part of the arm, and through this drop a single scratch, ⅛ inch (0.32 cm.) in length, was made by means of a sterile needle, care being taken not to draw blood. The mixture of vaccine and serum was then gently but thoroughly rubbed into the scratch with the side of the needle, and the wound was allowed to dry. Readings were made on the second, seventh and fourteenth days thereafter. In all but one of twenty-seven cases in which the dilution of the virus vaccine with the serum was less than 1 part of vaccine to 9 parts of serum, there was a definite "take," as evidenced by erythema, papules, vesicles or a pustular umbilication, with subsequent drying and scabbing of the area. With higher dilutions of the vaccine a "take" was uncertain, and there was no external evidence of a successful vaccination in the cases in which the amount of serum used was greater than twelve times the amount of virus vaccine. The children in whom the vaccination was successful showed little difference in the local or general reaction, whether the dilution of the vaccine with the serum was high or low.

From this experiment it is seen that vaccine virus retains its potency to produce regularly a successful vaccination when mixed with the serum of persons who have been vaccinated about five years previously, even when the concentration of vaccine virus to serum is as low as 12 per cent.

Experiment 2.—*Vaccination with Virus Diluted with Varying Proportions of Highly Potent Immune (Hyperimmune) Serum.*

The experiments in this series were identical with those of the previous group except that the diluting serum was of the hyperimmune type, being obtained from

5. Demme, Hans Z.: Variola-Vakzinestudien, Ztschr. f. Immunitätsforsch. u. exper. Therap. **55**:191, 1928.

two children who four weeks previously had a successful vaccination. The results of this experiment are in striking contrast to those of the first series. In this group of forty-two cases there was no evidence of a "take," as manifested by either local or general reaction, in any case in which the proportion of vaccine to immune serum was less than 1 part of vaccine to 3 parts of serum. In only one of five children did the vaccination "take" when the proportion of vaccine to serum was as 1:3; and a successful vaccination could not be obtained regularly until the amount of virus vaccine used was three times greater than the amount of immune serum.

It is seen from this experiment, in contrast to the first, that hyperimmune serum has a direct effect in preventing either the local or the general manifestations of vaccination when mixed with virus vaccine in suitable proportions.

Experiment 3.—Revaccination of Subjects Previously Giving Negative Reactions.

The next step was to determine whether the children studied in experiment 2 who showed no cutaneous or general reaction when vaccinated previously were immune to vaccinia, as determined by revaccination with potent vaccine virus. In recording the revaccination reactions two factors were considered: first, the "sensitivity" reaction, i. e., an early reaction reaching full development within the first forty-eight hours after revaccination and indicating merely a sensitivity induced by the previous vaccination, and, second, the character of the resulting vesicle formation, it being recognized that any existing immunity tended to depress the subsequent revaccination reaction. The greater the immunity the sooner such a reaction is aborted; and in persons who have complete immunity the infectious process may be extinguished without visible evidence of a reaction. It was thought formerly that the early reactions were highly dependable as indexes of immunity to vaccinia or to smallpox; however, McKinnon and Defries,[6] among others, have shown that this is not the case, this reaction giving evidence of a previous vaccination or infection with smallpox but no direct evidence of the degree of the immunity.

Three months after the original vaccination, eight of the children of experiment 2 who previously showed a negative reaction were revaccinated on the opposite arm with undiluted virus vaccine just tested for potency. The method used was identical with the one originally employed. The children were then seen on the second, seventh and fourteenth days after vaccination. None of them showed evidence of having developed any immunity at this period. All gave definite vaccination reactions, although in two the local lesion appeared rather early, crusting having already begun by the end of the first week. In two there was a moderate systemic reaction during the early period of the vaccinia.

The second group of revaccinated children (sixteen) were retested six months after the original vaccination, with the idea that the production of immunity was a slow process when mixtures of virus and immune serum were employed. However, these children, as a group, also failed to show definite evidence of an acquired immunity.

In three of these children there remained at the site of inoculation at the end of the seventh day a small red papule, about 1 or 2 mm. in diameter; there was no redness about it nor was there pain or tenderness. At the end of two weeks

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6. McKinnon, N. E., and Defries, R. D.: Interpretation of Reactions Following Re-Vaccination, Canad. Pub. Health J. **22**:33 (Jan.) 1931.

this either had almost disappeared or remained as a scar the size of a pinpoint. All the other children gave a typical vaccination reaction, although in only one was there a systemic reaction. Of the three children who were apparently immune on revaccination, two had been vaccinated originally with equal parts of vaccine and serum; the other was originally vaccinated with 3 parts of vaccine and 1 part of serum.

A third group of fourteen children was revaccinated after nine months, with practically the same results as were noted in the preceding series. One child gave no evidence of reaction, and on a subsequent revaccination again gave a negative reaction. Two other children gave very small reactions, as described for the preceding series. The other eleven showed local reactions of normal severity, although, again, systemic reactions were not noted. The two children in whom the reaction was mild were originally vaccinated with 2 parts of vaccine and 1 part of serum. The original dosage used for the other cases varied from 3 parts of vaccine to 1 part of serum to equal parts of vaccine and serum.

COMMENT

From the experiments described it can be deducted that immune serum, i. e., the blood serum of persons recently vaccinated, has a definite inhibiting effect on the action of vaccine virus when mixtures of the two substances are inoculated into the skin of subjects who are not immune. With such mixtures a definite local vaccination reaction is not regularly produced until the amount of vaccine is three times that of the serum, and in all instances in which the amount of diluting serum is three times greater than that of the vaccine employed, a local vaccination reaction is regularly inhibited. As a control experiment, using as a diluting substance for the vaccine a serum having little or no immune properties, it was noted that typical vaccination reactions were regularly produced in all cases in which the concentration of the vaccine to the diluting serum was greater than 11 per cent, or 1 part of vaccine to 9 parts of serum.

Reasoning from the results obtained with toxin-antitoxin mixtures in diphtheria and from the results of experiments with vaccine virus-immune serum mixtures, both in vitro and in animals, it seemed reasonable to expect that vaccination with such mixtures would be productive of a gradually developing immunity, even though no local lesion was produced. This, however, has not been the case. The majority of children so vaccinated have, on revaccination with potent undiluted virus vaccine, shown a definite vaccinia, even though as long a period as nine months elapsed between the original injection and the revaccination. In the small number of children in whom such a virus-immune serum mixture produced immunity, there could not be definitely determined a quantitative relationship between the amount of virus vaccine employed and the diluting immune serum. It is possible that in man the slow release of small amounts of vaccine virus is not a sufficient

stimulus to effect the production of general immunity. This would explain the negative results obtained here in the face of considerable experimental evidence to the contrary in animals.

SUMMARY

Potent immune serum, when mixed with vaccine virus in definite proportions, is regularly capable of inhibiting the development of the local lesion of vaccination.

Persons vaccinated with immune serum-virus vaccine mixtures in whom no local lesion has been produced are not usually immune to vaccinia, as determined by their reaction to a subsequent vaccination with potent undiluted virus vaccine.

EXCRETION OF DRUGS IN MILK

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This is the third paper from the laboratory of Cornell University Medical College dealing with the elimination of drugs in human milk.[1] Reed [2] presented an excellent review of the literature up to 1908; Joachimovits [3] gave a bibliography of about twenty-five references. Terwilliger and Hatcher [1b] have discussed the literature briefly, and we shall discuss only a few papers dealing with the subject.

Recently Joachimovits employed the Hanauer analytical lamp for the detection of traces of numerous substances in milk, but his investigation was limited to substances which are fluorescent, and it is interesting chiefly because his method permits of the detection of traces of many substances in the mother's milk. He made no quantitative determination of any of these substances.

Van der Bogert [4] reported the case of an infant in whom a papulopustular eruption developed which was attributed to bromide in the milk of the mother, who was taking bromides. Chemical examination showed that the milk contained "more than traces" of bromide. Frensdorf [5] reported that the cumulative action of phenobarbital was manifested in an infant whose mother, who was epileptic, took 0.8 Gm. in three days. The infant could be aroused only with difficulty. Careful examination of the data submitted by Frensdorf leaves doubt in our minds whether the condition of the infant was due solely to the phenobarbital excreted in the milk, because the depression became severe after only small amounts of milk had been taken.

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1. (*a*) Hatcher, R. A., and Crosby, Hilda: The Elimination of Nicotin in the Milk, J. Pharmacol. & Exper. Therap. **32**:1, 1928. (*b*) Terwilliger, W. G., and Hatcher, R. A.: The Elimination of Morphine and Quinine in Human Milk, Surg., Gynec. & Obst. **58**:823 (May) 1934.

2. Reed, C. B.: A Study of the Conditions that Require the Removal of the Child from the Breast, Surg., Gynec. & Obst. **6**:514, 1908.

3. Joachimovits, R.: Nachweis von Medikamenten und Giften in Muttermilch und Fruchtwasser mittelst Lumineszenz—Analyse, Monatschr. f. Geburtsh. u. Gynäk. **83**:42 (Sept.) 1929.

4. Van der Bogert, F.: Bromin Poisoning Through Mother's Milk, Am. J. Dis. Child. **21**:167 (Feb.) 1921.

5. Frensdorf: Uebergang von Luminal in die Milch, München. med. Wchnschr. **73**:322 (Feb. 19) 1926.

Since no determination has been made of the amounts of many commonly used drugs excreted in human milk, we have undertaken such a study with a view to estimating, as far as possible, the concentrations in which they occur in milk after the administration of therapeutic doses, or at least determining whether they are present in amounts sufficient to cause injury to the normal nursing child. We used the milk of patients in the obstetric wards of the Lebanon and Morrisania City hospitals, obtained from the third to the ninth day after delivery. The dosage of every drug, except phenophthalein, was in grains or fractions of a grain, but we have expressed it in the approximate equivalent in the metric system. One patient received morphine sulphate by subcutaneous injection. The others received oral doses of one of the following drugs: codeine, sodium salicylate, phenolphthalein, barbital, sodium bromide and potassium iodide. In every case the milk was pumped from the breast immediately before the administration of the drug and after varying intervals following the administration. The volume of the several specimens of milk varied from 17 to 127 cc. In every case control experiments were conducted with cow's milk in order to determine the suitability of the technic employed. Chloroform U. S. P. (containing about 2 per cent by volume of alcohol) was used for the extraction of morphine; in all other cases we used chloroform from which nearly all the alcohol had been removed.

CONTROL EXPERIMENTS

The morphine was extracted by the method described by Terwilliger and Hatcher. Codeine was recovered after the addition of 7.16 mg. of codeine sulphate to 100 cc. of cow's milk. The milk was rendered alkaline by the addition of sodium hydrate and was shaken with about twenty times its volume of chloroform. The remainder of the procedure is the same as that for the colorimetric estimation of morphine by means of Marquis' reagent.[6]

One milligram of sodium salicylate was added to 50 cc. of cow's milk; the milk was acidulated with sulphuric acid and shaken with twenty times its volume of chloroform. The chloroform was filtered, and the filtrate was distilled. The residue was treated with a little alcohol, which left the fat undissolved. A few drops of the alcohol gave a typical purple reaction with ferric chloride. The amount of salicylic acid present in the extract was determined approximately by comparing the intensity of the color produced by ferric chloride with that afforded by a dilute solution containing a known amount of salicylic acid. The addition of a few drops of dilute solution of ferric chloride to 25 cc. of cow's milk to which 1 mm. of sodium salicylate had been added afforded a distinct reaction for salicylate.

The addition of sodium hydrate to milk containing 1 part of phenolphthalein in from 3,000,000 to 4,000,000 parts of milk (varying with different specimens) gave a

6. Gauss, H.: Colorimetric Method for the Estimation of Morphine in Colloidal Mixtures and Tissues, J. Lab. & Clin. Med. **6**:699 (Sept.) 1921.

distinct tint, and the amount could be determined roughly by comparing the color induced in the specimen with that induced in milk containing known amounts of phenolphthalein.

Specimens of milk were tested for barbital by the method of Koppanyi and his co-workers,[7] which depends on the use of a cobaltous salt. In one control experiment 1 mg. of barbital was detected in 25 cc. of cow's milk, and in another, 1 mg. of sodium amytal in 25 cc. of human milk.

The method described by Autenrieth and Warren[8] was used for the estimation of bromide in milk. It depends on the liberation of bromine from the ash of the milk by the use of sulphuric acid in the presence of potassium permanganate, the removal of the bromine by shaking with chloroform and comparison of the chloroformic extract with that of a chloroformic solution containing a known amount of bromine. By this means the presence of bromine was shown after the addition of 1 mg. of sodium bromide to 25 cc. of human milk.

The presence of iodide was detected after the addition of 1 mg. of potassium iodide to 25 cc. of cow's milk by the following method: The milk was evaporated, and nitric acid was added; the mixture was shaken with chloroform, and sodium hydrate was added to the separated chloroform to the point of decolorization. The aqueous solution was purified by adding concentrated nitric acid and shaking with chloroform. The amount of iodine in the chloroformic solution was determined (approximately) by comparing it colorimetrically with a chloroformic solution of iodine of known concentration.

RESULTS

Codeine Sulphate.—Each of two patients was given 65 mg. of codeine sulphate, and the breasts were emptied four hours later. The specimens of milk measured 24 and 46 cc., respectively. One woman received a total of 130 mg. in two doses of 65 mg. each, given two hours apart. A specimen of milk measuring 127 cc. was drawn two hours after the last dose. A total of 192 mg., in doses of 32 mg. every four hours, was administered to each of two patients, and specimens of milk measuring 18 and 55 cc., respectively, were drawn four hours after the last dose. Not a trace of codeine was detected in any of the five specimens.

Morphine Sulphate.—S. G., aged 30, who had had a stillborn child, and who was suffering from gallbladder colic, was given 16 mg. of morphine sulphate hypodermically. A specimen of milk measuring 17 cc., drawn four hours later, contained at most only a trace of morphine, certainly less than 0.1 mg., and probably much less than that, since the color reaction was atypical.

Sodium Salicylate.—A total of about 4 Gm. (60 grains) of sodium salicylate was given to a nursing woman in doses of 640 mg. (10 grains) every four hours. Three others received sodium salicylate in doses of

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7. Koppanyi, T.; Murphy, W. S., and Krop. S.: Colorimetric Detection of Barbital and Its Application, Proc. Soc. Exper. Biol. & Med. **30**:542 (Jan.) 1933.

8. Autenrieth, W.: Laboratory Manual for the Detection of Poisons and Powerful Drugs, translated by W. H. Warren, ed. 6, Philadelphia, P. Blakiston's Son & Co., 1928.

320 mg. (5 grains) every four hours, and the following total amounts: One received about 2 Gm. (30 grains), another 1.2 Gm. (20 grains), and another 0.6 Gm. (10 grains). In every case the milk was collected four hours after the last dose. The specimens measured 31, 26, 22 and 12 cc., respectively. The extracts of the first and second specimens contained 1 mg. of salicylic acid; the third contained about 0.25 mg., and the last contained the barest trace, probably not more than 0.02 mg.

Sodium salicylate was administered to several other patients, and the milk was examined, but while these specimens almost certainly contained traces of salicylic acid, we failed to detect it because of the use of a slight excess of ferric chloride which obscures the reaction. When only traces of salicylic acid are present, it is necessary to avoid the use of more than minute amounts of very dilute solution of ferric chloride. Since no reaction was perceptible in any case after the addition of a dilute solution of ferric chloride directly to the milk, none of these specimens contained so much as 1 part of salicylate in 25,000 parts of milk.

Phenolphthalein.—This drug was administered in single doses to each of five patients, and specimens of milk were drawn after intervals of six, twelve and eighteen hours in every case. Two of the patients received laxative doses of 30 mg. of phenolphthalein; one received a dose of 60 mg., and two received doses of 90 mg. Not one of the fifteen specimens of milk afforded a trace of pink color after the addition of sodium hydrate. If any phenolphthalein was present in the milk, the concentration was less than 1 : 3,000,000, or less than 0.03 mg. per hundred cubic centimeters of milk. This could not exert any perceptible action in a normal infant.

Barbital.—This drug was given to each of two women in a dose of 325 mg., and to each of two others in a dose of 650 mg. A specimen of milk was drawn after an interval of six hours in every case. Not a trace of barbituric acid could be detected in any case; hence there was less than 1 part of barbiturate in 25,000 parts of milk, and if any was present it was insufficient to cause narcosis, such as Frensdorf described.

Sodium Bromide.—A total of 15 Gm. of sodium bromide was administered to each of two patients in doses of 1 Gm. five times daily. A total of twenty-one specimens of milk was drawn within six days after the first dose. The volume of these specimens varied from 40 to 120 cc. The first specimen from one patient and the first and second specimens from the second patient did not yield any bromide, but in every one of the remaining eighteen specimens bromide was found; the largest amount recovered, approximately 8 mg., was obtained from a specimen which measured 120 cc., but each of the greater number of specimens yielded

about 2 mg. These results indicate that mild symptoms of brominism, such as Van der Bogert reported (eruptions), may result in susceptible infants after the administration of large doses of bromides to the mother.

Potassium Iodide.—A total of 3.6 Gm. of potassium iodide was administered in doses of 325 mg. given three times daily to a young primiparous patient, and a total of 4.6 Gm. was administered to a young multipara in doses of 650 mg. three times daily. Specimens of milk measuring 30 and 35 cc., respectively, were obtained from the first patient after the eighth and eleventh doses, and one specimen measuring 26 cc. was obtained from the second patient two hours after the last dose. All three specimens contained iodide, the amount being too small to measure accurately, but in every case it was of the order of 1 mg.

SUMMARY

Morphine could not be detected with certainty in the milk of a woman who had received 16 mg. of the sulphate hypodermically.

No codeine could be recovered from any specimen of milk after doses varying from 32 to 65 mg.

Salicylic acid was detected in every one of four specimens of milk (there being approximately 1 mg. in one specimen) following the administration of total amounts of 0.6, 1.2, 2 and 4 Gm. of sodium salicylate. We failed to detect it in several cases in which traces were almost certainly present, but we attribute this to the use of too much ferric chloride in testing the extract.

No evidence of phenolphthalein in the milk was obtained even after a dose of 90 mg., although as little as 0.03 mg. per hundred cubic centimeters of milk could have been detected with certainty.

No evidence could be found of the presence of barbital in any specimen of milk, even after doses of 650 mg. of barbital.

After the administration of sodium bromide in single doses of 1 Gm. and total doses of 15 Gm., every specimen of milk, except the first in one case and the first and second in another, yielded bromide. In one case the amount present was sufficient to suggest that the continued use of such milk might cause mildly toxic symptoms in an infant.

Two specimens of milk obtained after a total of 3.8 Gm. of potassium iodide and one after a total of 4.6 Gm. of potassium iodide contained only extremely small amounts of iodide.

None of the drugs, except sodium bromide, was present in the milk in an amount sufficient to indicate that the continued use of such milk would injure a normal nursing child.

TEETH IN FETAL RICKETS

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The important lesions of rickets, whether caused by a deficiency of vitamin D or by an extreme deficiency of calcium, are to be seen in the calcified structures of the body. The most highly calcified structures of the body are the teeth. Enamel, according to von Bibra,[1] consists of approximately 96.41 per cent inorganic substance and 3.59 per cent organic substance, and dentine, of 72.39 per cent inorganic and 27.61 per cent organic substance. It is to be expected, therefore, that disturbances of calcium metabolism will affect the process of calcification of the teeth.

The association of rickets with defective structure of the teeth has long been recognized clinically, but detailed knowledge of the lesions has awaited the experimental production of these defects. Without doubt the most comprehensive study of rickets and the associated dental lesions has been made by Mellanby.[2] In her report were described the effect on the structure of the teeth of variations in the amount of vitamin D and variations in the calcium-phosphorus ratio of the diet. The conclusion was that the amount of calcium and the calcium-phosphorus ratio are of little significance as compared with the vitamin D factor.

Rickets occurs usually between the fourth month and the second year of life; hence defects of the permanent teeth are common, because calcification of these teeth takes place within this period. Gross hypoplasia of the deciduous teeth is, however, extremely rare. Dick [3] stated that in a careful search during a long period for a hypoplastic condition of the milk incisor teeth both of school children and of infants who attended the Hackney Mothers Center he failed to detect it in a single case. He concluded as a result of these investigations that the fetus is immune to rickets. On the other hand, Mellanby [4] stated that micro-

From the Division of Dental Surgery, Department of Surgery, Peiping Union Medical College.

1. von Bibra, quoted by Mummery, J. H.: The Microscopic and General Anatomy of the Teeth, in Christian, H. A., and Mackenzie, J.: Oxford Medicine, ed. 2, New York, Oxford University Press, 1924.

2. Mellanby, May: Diet and the Teeth: An Experimental Study, Medical Research Council, Spec. Rep. Ser. 140, London, His Majesty's Stationery Office, 1929, pt. 1.

3. Dick, J. L.: The Teeth in Rickets, Proc. Roy. Soc. Med. (Sect. Odont.) **9**:83, 1916.

4. Mellanby, May, quoted by Toverud and Toverud.[5]

scopic changes are present in 80 per cent of all deciduous teeth. The Toveruds [5] were unable to find rickets, as judged by the usual clinical methods, in any new-born infants. However, they described a case of hypoplasia of the deciduous incisors in a boy 5 years old and stated that the diet of the mother during the period of pregnancy was markedly deficient in calcium. That fetal rickets exists has been demonstrated amply by Maxwell.[6] Since the publication of his observations in 1930, fourteen additional cases have been studied and will be reported by him.

The only description of the dental structure in fetal rickets was made by Anderson in the report of one of Maxwell's [6b] cases. He described a calcified section of a developing incisor tooth. The calcifying border of the dentine was irregular in outline, the odontogenic zone was wider than normal, and the decalcified enamel showed some abnormality of staining.

Case 1 is reported because to my knowledge it is the first instance in which an opportunity to study the erupted teeth of a patient with a proved case of fetal rickets has presented itself. Cases 2 and 3 are cases of stillborn infants whose mothers suffered from osteomalacia.

REPORT OF CASES

CASE 1.—Chin Ming, a girl, was the first child of a woman aged 19 who was admitted to the hospital in an emergency. She had been in labor for ten hours. The significant point in the history was that during the previous month there had been several attacks of carpopedal spasm daily, each lasting for a few minutes. Examination at the time of admission revealed positive Chvostek and Trousseau signs. The blood calcium was 5.4 per hundred cubic centimeters of serum, and the phosphorus, 2.9 mg. A roentgenogram showed no definite evidence of osteomalacia. The woman had a spontaneous and normal delivery.

Roentgen examination of the bones of the infant revealed mild but definite rachitic changes of the epiphyseal ends of the long bones. The blood calcium was 8.1 mg. per hundred cubic centimeters, and the phosphorus, 4.2 mg.

The infant was fed mother's milk, supplemented with goat's milk; cod liver oil and cabbage soup were given, and the child was kept in the sun from one to two hours daily.

The infant was next seen when 9 months old. She was said to have lifted her head at the age of 3 or 4 months and to have sat up with assistance when 7 months old. No teeth were erupted at that time. Roentgenograms showed a regression of the rachitic changes in the long bones. The child had been well except for an infection of the upper respiratory tract.

At 20 months of age the child was admitted to the hospital with bronchopneumonia. Apart from the changes in the chest, examination revealed a suggestive

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5. Toverud, K. U., and Toverud, G.: Studies on Mineral Metabolism During Pregnancy and Lactation and Its Bearing on Disposition to Rickets and Dental Caries, Acta pædiat. (supp. 2) **12**:1, 1931.

6. Maxwell, J. Preston: (*a*) Osteomalacia and Foetal Rickets, Brit. J. Radiol. **3**:375 (Aug.) 1930; (*b*) Two Cases of Foetal Rickets, J. Path. & Bact. **33**:327, 1930.

Harrison groove but no enlargement of the costochondral junctions. A roentgenogram showed no evidence of rickets. At this time casts were made of the teeth, and one upper incisor was extracted for histologic study.

The following teeth were erupted: $\frac{IV\ \ III\ \ II\ \ I/I\ \ II\ \ III\ \ IV\ \ III/III}{IV\ \ \ II\ \ I\ /\ I\ \ II\ \ \ IV}$ incompletely. There appeared to be normal enamel on the incisal third of the incisor teeth (fig. 1) and absence or extreme hypoplasia of enamel on the incisal tip of the canines and of the occlusal third of the first deciduous molar.

In a normally developing fetus calcification begins in the incisor tooth germs at approximately the seventeenth week. At the twentieth week (fig. 2) calcification of the tip of the central and lateral incisors has occurred. By the twenty-fourth week calcification has commenced in the cusps of the second molar and in

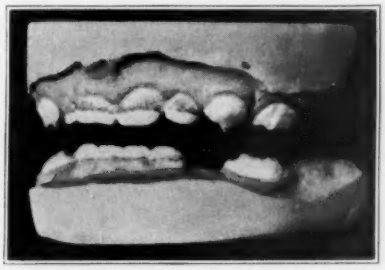

Fig. 1 (case 1).—Models of teeth, showing normal enamel of the incisal third of the incisor teeth and hypoplasia of the occlusal surface of the molar and the tip of the canine teeth.

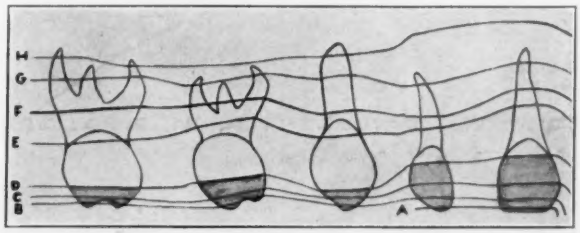

Fig. 2.—A chart representing the calcification period of the deciduous teeth. *A* shows the development at the fetal age of 20 weeks; *B*, at 24 weeks; *C*, at 33 weeks; *D*, at birth; *E*, at 8 months; *F*, at 12 months; *G*, at 18 months, and *H*, at 2 years. (From Tomes, C. S.: Manual of Dental Anatomy, ed. 8, Philadelphia, P. Blakiston's Son & Company, 1923.)

the tip of the canines. At birth most of the crown of the incisors is calcified. Correlating the deficiencies in the teeth of this patient with the period of calcification of the teeth, it may be inferred that calcification began normally at the seventeenth week and proceeded until the twenty-third week (the incisal enamel is seen in figure 3 to be well formed). From this time on calcification was extremely poor, as seen by the marked hypoplasia of the enamel and the absence of enamel from the lingual surface of the incisors. Normal calcification was resumed at the period corresponding approximately to the first week of extra-uterine life, when the rachitic condition was recognized and appropriate treatment was given. The

line separating the hypoplastic from the normal enamel was sharp and was indicative of the rapid response of the enamel organ to the improvement in the nutrition of the infant. This rapid response was in accord with the observations of Mellanby in experimental rickets.

The enamel formed last (during the fifth and sixth months of extra-uterine life) was somewhat hypoplastic. One may infer that the nutrition of the infant suffered at this time, but the record gave no information on this point.

This patient had fetal rickets, proved at birth by roentgenogram, and at the time of writing this report shows no clinical evidence of rickets. The teeth, however, show gross and microscopic changes characteristic of rickets. From the histologic picture the period at which the deficiency occurred in utero can be stated.

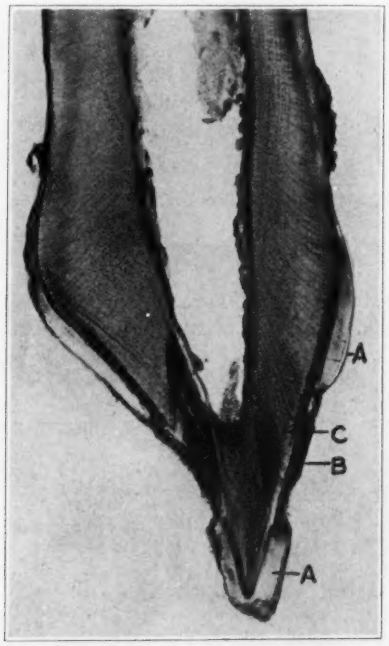

Fig. 3 (case 1).—A ground section of an incisor tooth, showing: *A*, normal enamel; *B*, hypoplastic enamel, and *C*, hypoplasia of the dentine.

CASE 2.—Mrs. Chang Teng-ke, a primipara aged 25, was admitted to the hospital in an emergency, having been in labor for four days. A diagnosis of fetal death was made, and embryotomy was performed immediately.

The mother's blood calcium was 8.3 mg. per hundred cubic centimeters of serum, and the phosphorus, 2.2 mg. Roentgen examination revealed osteomalacia with marked contraction of the pelvic bones.

Autopsy on the infant showed a slight irregularity of the lines of ossification, especially marked at the lower end of the femur and the upper end of the humerus. Microscopic examination revealed definite rachitic changes.

In a decalcified section of the jaw bone (fig. 4) the bone trabeculae were seen to be bounded by wide zones of osteoid tissue which took a pale pink stain. A

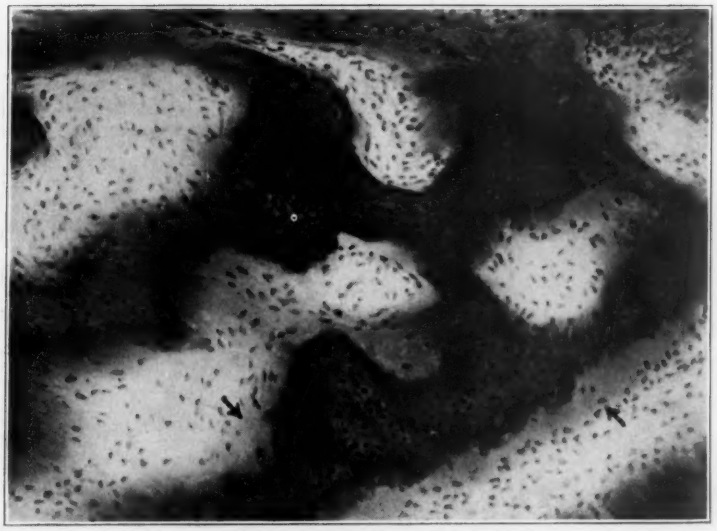

Fig. 4 (case 2).—A decalcified section of the maxilla. The arrows point to the osteoid.

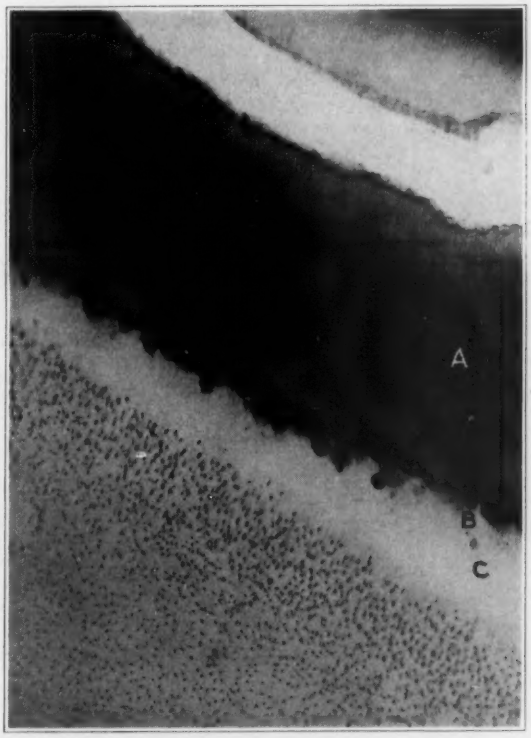

Fig 5 (case 2).—A decalcified section of an incisor tooth, showing: *A*, the uneven staining of the dentine; *B*, the irregular calcifying border, and *C*, the wide odontogenetic zone.

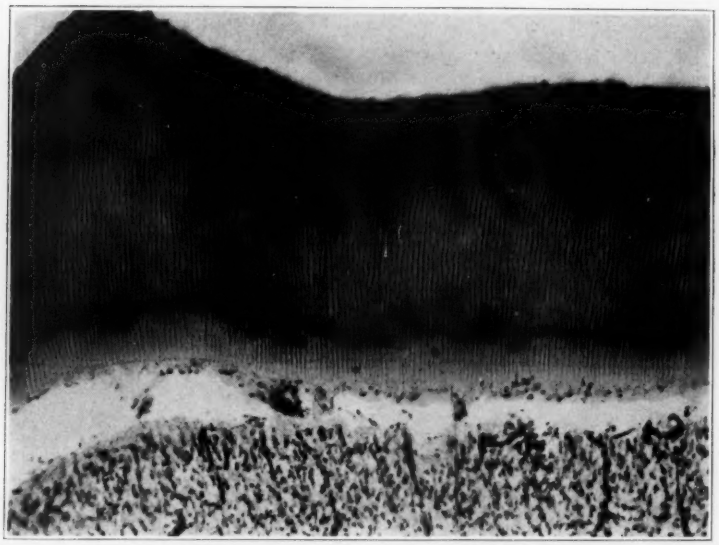

Fig. 6 (case 3).—A decalcified section of an incisor tooth showing the dentine border (*A*).

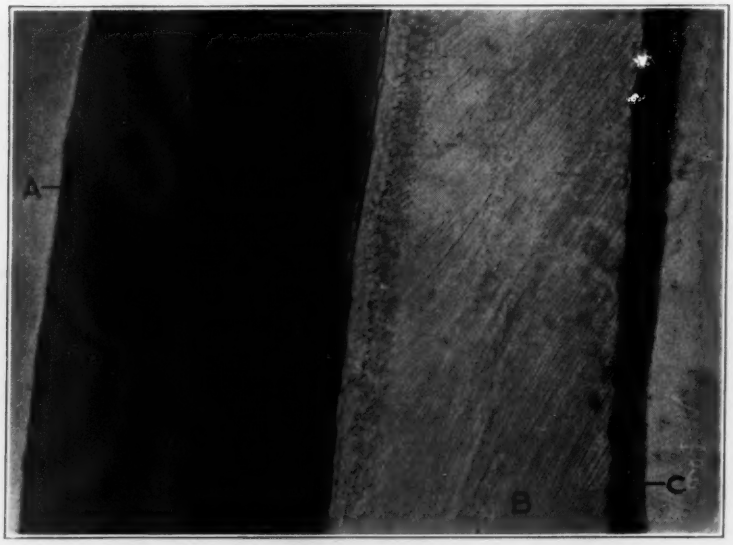

Fig. 7 (case 3).—A ground section of an incisor tooth, showing: *A*, the enamel; *B*, the dentine, and *C*, the odontogenetic zone.

decalcified section of the developing incisor tooth showed marked irregularity of calcification as seen by uneven staining throughout. The outline of the forming border of the dentine was very irregular, and the predentine layer was much wider than normal. Islands of blue-staining material (calcoglobulin) were scattered along the zone of calcification.

The diagnosis was fetal rickets affecting the teeth.

CASE 3.—A tertipara, 24 years of age, gave a history of pain and spasms of the muscles of the legs for five years following the birth of her first child. Examination revealed osteomalacia with tetany. Carpopedal spasm and Chvostek and Trousseau signs were present. A diagnosis of pregnancy at term, osteomalacia, tetany and pyorrhea alveolaris was made. The blood calcium was 7.8 mg. per hundred cubic centimeters; the phosphorus, 3.87 mg.; the albumin, 2.91 mg., and the globulin, 2.59 mg.

The infant, delivered by cesarean section, was stillborn. The serum calcium was 5.56 mg. per hundred cubic centimeters, and the phosphorus, 4.2 mg. Roentgenograms showed moderate rachitic changes in most of the long bones, with flaring, irregularity and cupping of the diaphyseal ends, particularly evident at the distal ends of both ulnas. Slight rachitic involvement was seen at both knee-joints.

A decalcified section (fig. 6) of an incisor tooth showed changes similar to those seen in case 2. There was marked irregularity of the calcifying border with widening of the odontogenic zone. Islands of calcoglobulin were seen scattered along the calcifying border. A ground section of another tooth showed uneven staining of the enamel. Rows of interglobular spaces were seen at some distance from the dento-enamel junction. The irregularity of the dentine border is well shown in figure 7. The tissues were in a poor state of preservation because the fetus had been dead for some time before delivery.

The diagnosis was fetal rickets affecting the teeth.

SUMMARY

Rickets occurring in the fetus manifests itself in the teeth by gross hypoplasia of the enamel.

The changes in the structure of the teeth give information regarding the period of greatest deficiency of calcifying factors.

While the bony changes may disappear so that there is no evidence of previous rickets, the changes in the teeth are permanent and remain as indelible evidence of the disease process.

DERMAL ABSORPTION OF VITAMIN D

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The purpose of this study was to determine whether the skin is capable of absorbing vitamin D in sufficient amounts to prevent and to cure experimental rickets.

A study of the literature shows a paucity of available information as regards the absorption of vitamin D through the skin. In 1926, Price [1] mentioned that vitamin D may be absorbed directly through the skin, but he offered no experimental proof. Hume, Lucas and Smith,[2] in 1927, were able to protect rats and rabbits against rickets by inunction with irradiated impure cholesterol. Moncorps et al [3] found that the absorption through the skin of large doses of irradiated ergosterol was followed by calcification of the aorta.

Rickets has previously been prevented and cured in one of two ways: (1) by the feeding of cod liver oil or of viosterol, or (2) by irradiation of the skin with the ultraviolet rays from sunlight or from artificial sources. A quantitative study to determine the amount of vitamin D necessary to prevent and heal rickets in experimental animals by absorption through the unbroken skin has not come to our attention. We therefore thought that it would be advantageous to obtain such data by animal experimentation.

INVESTIGATION

The scope of the present study was: (1) to determine whether inunction with viosterol prevents experimentally produced rickets; (2) to determine whether inunction with vitamin D cures experimentally produced rickets; (3) to determine whether the dosage of viosterol used produces symptoms of hypervitaminosis, and (4) to ascertain whether the effect produced by inunction is due to the direct absorption of vitamin D or to the activation of the viosterol in the skin by secondary irradiation.

From the pathological service, Menorah Hospital; Dr. Robert Koritschoner, Director.

1. Price, W. A.: Indust. & Engin. Chem. **18**:670, 1926.
2. Hume, E. M.; Lucas, N. S., and Smith, H. H.: Biochem. J. **21**:362, 1927.
3. Moncorps, C., et al.: München. med. Wchnschr. **80**:1289 and 1482, 1933.

PROCEDURE

White albino rats weighing between 50 and 70 Gm. were chosen for the experiments. The life cycle of these animals being short, rachitic manifestations in the bones may be produced in a relatively short period of time, and the effects of therapy may be observed over a correspondingly short interval. The animals were of the same age, and as many as possible were taken from the same litters. Each animal was kept in a separate cage. The hair on the portion of the abdominal wall chosen for inunction was carefully removed by a depilatory,[4] so as to avoid the minute cuts and scratches incidental to shaving. A piece of adhesive tape, ½ by 1½ inches (1.27 by 3.8 cm.), was permanently fixed on each animal's back to act as an anchor for the bandage which protected the treated area. Great care was exercised in the selection of an area which the animal could not reach. The area receiving the inunction was then covered with a piece of gauze. Adhesive tape covered the gauze, and it was snugly wound around the animal's body and affixed to the permanent piece of tape. In this manner the bandage could be removed for the treatment without irritation of the skin. Access to the treated area on the part of the animal was not possible. A standard bandage was used for all of the animals. This bandage was put in place several days before the beginning of the experiment in order to accustom the animal to experimental conditions. Any effect due to the restriction of motion or to bodily discomfort was present in the controls as well as in the treated animals. After a period of forty-eight hours the animals became conditioned to the presence of the bandages and made no effort to free themselves.

As an inunction we made a compound of: yellow wax, 5 parts; spermaceti, 5 parts; viosterol in oil 250 D, 26 parts;[5] olive oil, 10 parts, and lecithin, 0.75 parts, in a cold cream base. This mixture contained 1,800 rat units[6] of vitamin D per gram. Another compound using an irradiated mineral oil instead of viosterol was employed to determined the mechanism of the action of vitamin D by inunction. This preparation of an irradiated mineral oil is known to be a source of secondary radiation in that it is capable of fogging a photographic plate.

The animals were divided into four groups of three animals each. The animals of group 1 were used as controls. They were placed on a normal diet of lettuce, carrots, bread, milk and water. These animals received no treatment.

The animals comprising groups 2, 3 and 4 were maintained on the Steenbock rachitogenic diet no. 2965. This diet consists of yellow corn, 76 per cent; wheat gluten, 20 per cent; calcium carbonate, 3 per cent, and sodium chloride, 1 per cent. It is devoid of vitamin D and has a high calcium and a low phosphorus content. Young rats placed on this diet over a period of three or four weeks invariably show rickets, provided every source of vitamin D is excluded.

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4. The preparation contained the sulphides of the alkaline earth-metals combined in a cold cream base.

5. Viosterol in oil 250 D, containing 0.62 mg. of activated ergosterol per cubic centimeter, which is equivalent to 3,333 rat units of vitamin D per gram by biologic assay.

6. A rat unit is defined as the amount of viosterol which when fed daily to a rachitic rat for ten successive days produces a wide line of deposit of calcium in the metaphyses of the distal ends of the radii and of the proximal ends of the tibias. This appears as a line of calcified tissue in the proliferative zone of the epiphyseal cartilage.

The rats comprising group 2 received by inunction every other day for thirty-five days 0.05 Gm. of the viosterol compound, containing 90 rat units, or a total of 1,620 rat units.

The animals in group 3 received by inunction 0.05 Gm. of the irradiated mineral oil every other day over a period of twenty-three days and then inunctions of 0.05 Gm. of viosterol every other day over a period of twelve days, or a total of 540 rat units.

The animals in group 4 were kept on the rachitic diet and received no treatment. These animals acted as a control for the determination of the efficacy with which rickets was produced by the diet.

Roentgenograms of all of the animals at the beginning of the experiment showed that they were free from rickets. Roentgenograms to determine the production of changes were made at the end of the twenty-third day. At the end of the thirty-fifth day, the animals were killed. A radius of each animal was split, stained with silver nitrate [7] and photographed. The silver nitrate reacts with the calcified portion of the bone to produce silver phosphate, which on exposure to light is stained black. The calcified portion of the bone appears black, while the uncalcified cartilage remains white (figs. 2, 4, 6 and 8).

RESULTS

Examination of the roentgenograms shows the bones of the animals fed the normal diet (group 1) to be normal (fig. 1). The arrows point to the normal osteochondral zones. The radius of a rat belonging to this group, as seen in figure 2, reveals no evidence of rickets. The head of the bone is narrow. The epiphysis and the diaphysis have a large deposit of calcium. The epiphyseal band is narrow, and the line of calcification is sharp.

The animals in group 2 were kept on the rachitic diet and received inunctions of viosterol every other day as previously described. In figure 3 is shown the roentgenogram of an animal in this group taken at the end of the twenty-third day, after the rat had received twelve treatments of 90 rat units each, or a total of 1,080 rat units. No evidence of rickets is to be seen. The arrows point to the normal osteochondral zones. Figure 4 is a section of the radius of an animal of this group made at the end of the period of thirty-five days. This animal received eighteen treatments of 90 rat units each, or 1,620 times the normal dose which, when taken internally, produces the McCollum "line test." [8] The bone appears normal. Large amounts of calcium may be seen in the epiphysis and in the diaphysis. The head of the bone shows no swelling. The cartilaginous layer of the epiphysis is narrow. The epiphyseal end of the shaft is sharply outlined.

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7. Stevens, H., and Nelson, E. M.: Indust. & Engin. Chem. (Anal. Ed.) **4**:200, 1932.

8. McCollum, E. V.; Simmonds, N.; Shipley, R. S., and Park, E. A.: J. Biol. Chem. **51**:41, 1922.

Fig. 1.—Roentgenograms of bones of a rat from group 1 receiving a normal diet and no treatment. The bones are normal. *A* shows the appearance at the beginning of the experiment; *B*, that after about four weeks. Arrows point to the normal osteochondral zones; no evidence of rickets is shown.

Fig. 2.—Section of the radius (× 10) of a rat from group 1 receiving a normal diet. The epiphysis and the diaphysis have a large deposit of calcium; the epiphyseal band of uncalcified cartilage is narrow, and the line of ossification is sharp. The narrow head of the distal end of the radius denotes a normal condition.

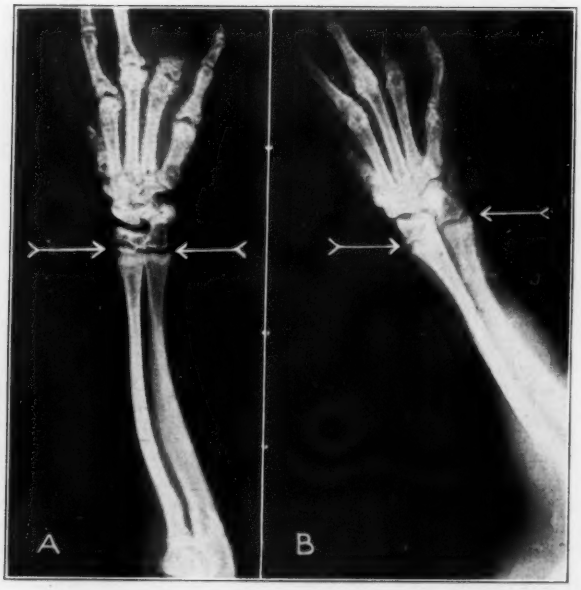

Fig. 3.—Roentgenograms of bones of a rat in group 2 placed on a rachitic diet and receiving inunctions of viosterol. The bones are normal. *A* shows the appearance at the beginning of the experiment; *B*, that, four weeks later. The normal osteochondral zones, indicated by arrows, and the clearcut lines of ossification denote that the animal was protected against rickets.

Fig. 4.—Section of the radius (× 15) of a rat from group 2 placed on a rachitic diet and receiving inunctions of viosterol for thirty-five days. The narrow head of the radius, the large deposit of calcium and the narrow zone of the cartilaginous layer of the epiphysis denote the absence of rickets.

In figure 5 are shown the roentgenograms of a rat in group 3. The animals in this series were kept on the Steenbock diet and received an inunction of 0.05 Gm. of irradiated mineral oil instead of viosterol every other day. The arrows point to the irregular increase in the width of the cartilaginous zone between the epiphysis and the diaphysis. There is a blurring of the ends of the metaphysis, denoting a disturbance in the chondral and the osseous development which is characteristic of rickets. These animals then received over a period of twelve days six

Fig. 5.—Roentgenograms of the radius and ulna of a rat from group 3 kept on a rachitic diet and receiving inunctions of irradiated mineral oil. *A* shows the appearance at the beginning of the experiment; the chondral and the osseous development are normal, as indicated by the regular cartilaginous zone between the epiphysis and the diaphysis. In *B*, showing the appearance four weeks later, the irregular increase in the width of the cartilaginous zone and the blurring of the ends of the metaphysis denote a disturbed chondral and osseous development, characteristic of rickets.

inunctions of viosterol of 90 rat units each, or a total of 540 rat units. In figure 6 is shown a section of the radius at the end of this treatment. Well advanced healing may be noted. The end of the bone is swollen, indicating that rickets had developed in this animal, as was

shown by the roentgenogram taken at the end of the twenty-third day. The uncalcified epiphyseal band is narrow. The cartilaginous metaphysis is calcified.

In figure 7 are shown the roentgenograms of a rat belonging to group 4. The animals in this group were kept on a rachitic diet but received no treatment. The bones show advanced rickets. The wide and irregular cartilaginous zone between the epiphysis and the diaphysis and the blurring of the epiphyseal end of the metaphysis are to be

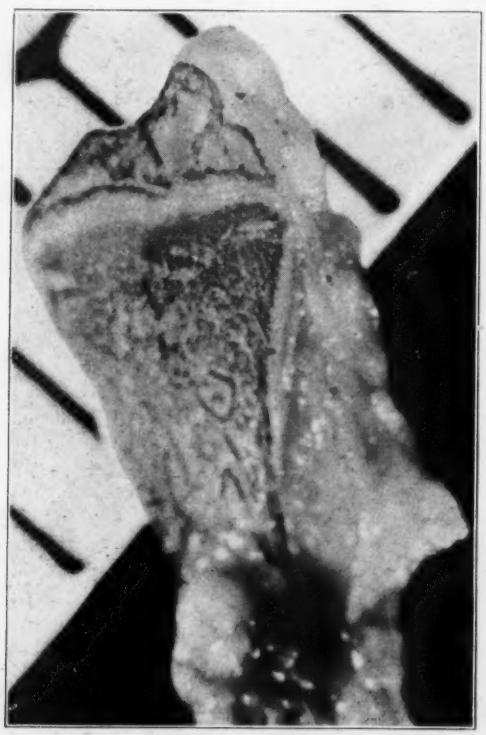

Fig. 6.—Section of the radius (× 15) of a rat in group 3 kept on a rachitic diet and receiving inunctions of irradiated mineral oil for twenty-three days and of viosterol for twelve days. The swollen head, the narrow uncalcified epiphyseal band and the calcified cartilaginous metaphysis denote well advanced rickets.

noted. It may be seen that the diet used was effective in producing rachitic changes in the bones. The radius of a rat belonging to this group is shown in figure 8. Definite evidence of rickets is indicated by the swelling of the head of the bone. The diameter of the head is to be compared with that of the shaft of the bone and with that of a normal head (fig. 1). There is a small deposit of calcium in the epiphysis and in the diaphysis, and the cartilaginous zone between the

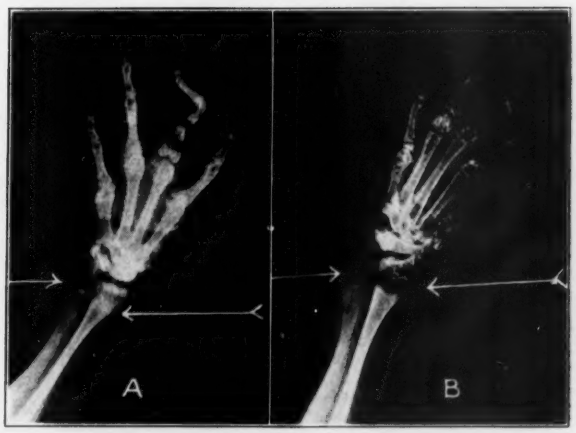

Fig. 7.—Roentgenograms of bones of an animal from group 4 kept on a rachitic diet but receiving no treatment. *A* shows the normal appearance before the experiment; *B*, advanced rickets, as denoted by the wider and irregular cartilaginous zone between the epiphysis and the diaphysis and the blurring of the epiphyseal end of the metaphysis.

Fig. 8.—Section of the radius (× 10) of an animal in group 4 kept on a rachitic diet and receiving no treatment. The diameter of the head should be compared with that of the normal bone in figure 2. The wide uncalcified epiphyseal band, the small deposit of calcium in the epiphysis and the incomplete ossification of the diaphysis denote advanced rickets.

epiphysis and the diaphysis is wide. There is no calcification of the epiphyseal cartilage and none in the metaphysis. The McCollum "line test" is negative. The end of the shaft is frayed out, irregular and hazy.

The results of these experiments are summarized in the table.

Prevention and Cure of Rickets by Inunctions of Viosterol

Group	Number of Animals	Diet	Treatment for Twenty-Three Days	Roentgenographic Findings	Treatment During Next Twelve Days	Results Seen in Macroscopic Section of Radius
1	10	Normal	None	Normal bone	None	Normal bone
	11	Normal	None	Normal bone	None	Normal bone
	12	Normal	None	Normal bone	None	Normal bone
2	4	Steenbock	Inunctions of viosterol	Normal bone	Inunctions of viosterol	Normal bone
	5	Steenbock	Inunctions of viosterol	Normal bone	Inunctions of viosterol	Normal bone
	6	Steenbock	Inunctions of viosterol	Normal bone	Inunctions of viosterol	Normal bone
3	1	Steenbock	Inunctions of irradiated mineral oil	Advanced rickets	Inunctions of viosterol	Healed rickets
	2	Steenbock	Inunctions of irradiated mineral oil	Advanced rickets	Inunctions of viosterol	Healed rickets
	3	Steenbock	Inunctions of irradiated mineral oil	Advanced rickets	Inunctions of viosterol	Healed rickets
4	7	Steenbock	None	Advanced rickets	None	Advanced rickets
	8	Steenbock	None	Advanced rickets	None	Advanced rickets
	9	Steenbock	None	Advanced rickets	None	Advanced rickets

DISCUSSION

It is readily seen from studies of the roentgenograms and from the macroscopic sections (figs. 3 and 4) that white rats may be protected against experimental rickets by inunction with vitamin D. The results are similar to those obtained by the oral administration of this vitamin. A study of figures 5 and 7 shows that the diet used was effective in producing rickets in our animals. Similar rachitic changes are also shown by the sections made of the bones (figs. 6 and 8). Inunctions of viosterol were capable of producing healing in this group of animals displaying marked rachitic manifestations. Vitamin D by inunction not only prevented rickets but produced well advanced healing. Therefore, the experiments cited strongly suggest that the skin is capable of absorbing vitamin D.

Since the amount of vitamin D given by inunction is so much larger than that given orally, the question of hypervitaminosis must be considered. Kreitman and Moll [9] produced hypervitaminosis in rats by feeding excessive doses of viosterol. None of the toxic symptoms indic-

9. Kreitman, H., and Moll, T.: München. med. Wchnschr. **75**:637, 1928.

ative of hypervitaminosis, such as loss of weight, diarrhea and anorexia, were present in our series; in fact, all of the animals receiving the highest doses gained weight and showed no gastro-intestinal disturbances. Microscopic examination of the aorta and kidneys of these animals showed no calcification. The amount of viosterol used was therefore not excessive.

It has been shown by a number of investigators that large doses of vitamin D are necessary before signs of toxicity become manifest. Even enormous doses cannot produce toxic symptoms in experimental animals kept on a normal diet. As much as 80,000 times the therapeutic dose failed to produce toxic [10] symptoms in rats kept on a diet of milk and bread. Further experiments to determine the minimum dose necessary to produce hypervitaminosis by inunction are under way. The danger of hypervitaminosis is exceedingly slight if preparations of viosterol of a strength of 250 D are used. According to these experiments, rats can tolerate at least 1,620 times the oral therapeutic dose without showing toxic symptoms. On the basis of direct proportional ratios by weight, a man weighing 70 Kg. (154 pounds) may absorb by inunction 700,000 rat units. This is equivalent to 335 cc. of viosterol 250 D, or 1¾ gallons (66 liters) of viosterol 25 D, plus the internal consumption of a loaf of commercial vitamin D bread and a quart (946 cc.) of vitamin D milk daily. How much more can be tolerated is not yet certain. Experiments are in progress to determine this point. Preliminary reports indicate that enormous doses may be used by inunction without the production of symptoms of hypervitaminosis.

It has been shown that viosterol retains its activity [11] under oxidizing conditions but is decomposed by the mineral acids. If the hypervitaminosis is due to products of decomposition of viosterol, as has been suggested,[12] it is reasonable to assume that there is more probability of decomposition by the hydrochloric acid of the stomach than by exposure to air on the surface of the skin before absorption. Therefore, vitamin D applied by inunction should be less likely to produce hypervitaminosis than the same amount of vitamin D taken internally.

Viosterol applied by inunction might exert its action in one of two ways. It might be absorbed as such and find its way directly into the blood stream, or it might act as an activator of the ergosterol in the skin by secondary irradiation. If the latter were true, however, the irradiated mineral oil, which is capable of sending out secondary radiation, should have protected the animals in group 3 against experimental

10. Hoyle, J. C.: J. Pharmacol. & Exper. Therap. **38**:271, 1930; **40**:351, 1930.

11. Bills, C. E.: J. Biol. Chem. **64**:1, 1925.

12. Rosenheim, O., and Webster, T. A.: Lancet **2**:622, 1927.

rickets. The fact that the animals were not protected by inunction with this preparation indicates that the results obtained were probably due to the absorption of vitamin D through the unbroken skin in a manner similar to the absorption of other substances.

Furthermore, a parallel series of experiments[13] shows that the source of ergosterol is immaterial. The same results are obtained by inunction with any of the available sources of vitamin D, natural or synthetic.

CONCLUSIONS

1. Viosterol is absorbed through the skin in sufficient quantities to prevent and cure rickets.

2. No hypervitaminosis was produced by the large doses used in these experiments.

3. The action of viosterol by inunction appears to be by direct molecular absorption rather than by secondary irradiation.

4. Absorption of vitamin D seems to be independent of the source of the viosterol, whether natural or synthetic.

13. Morgen, R. A.: Unpublished data.

COMPLICATIONS OF VARICELLA

I. THEIR OCCURRENCE AMONG 2,534 PATIENTS

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Chickenpox is the disease of childhood which is taken least seriously by the laity and by the medical profession. The illness is usually so lightly considered that no treatment is deemed necessary, and ordinary precautions to prevent its spread are omitted. At the Willard Parker Hospital we encountered so many and so varied a group of complications among patients with varicella that the present study was undertaken to determine their frequency and character.

The study includes the cases of the 2,534 patients with varicella seen at the Willard Parker Hospital during the five-year period from Jan. 1, 1929, to Dec. 31, 1933. One hundred and thirty-three patients, or 5.2 per cent, suffered from some type of complication. For a number of reasons the incidence of complications would be higher in a group of hospitalized patients than among patients kept at home. The occurrence of a more or less serious complication in 5 per cent of the patients admitted to the hospital indicates that the disease is far less innocuous than is usually believed.

The complications in the order of frequency were:

Complication	Patients	Complication	Patients
Otitis media	37	Laryngitis	3
Abscess	24	Meningitis	3
Pneumonia	21	Empyema	3
Lymphadenitis	16	Nephritis	3
Cellulitis	15	Herpes zoster	3
Septicemia	14	Osteomyelitis	2
Erysipelas	7	Balanitis	2
Encephalitis	5	Pericarditis	1
Appendicitis	5	Endocarditis	1
Gangrene	4	Hordeolum	1
Mastoiditis	4	Severe pharyngitis	1
Impetigo	4	Blepharitis	1
Intestinal intoxication	3	Stomatitis	1
Paronychia	3	Parotitis	1
Conjunctivitis	3		
Total			191

Forty-one patients suffered from more than one complication.

Hospitalized children are prone to have certain diseases, especially otitis media, regardless of the original cause of admission. In an attempt to determine the degree of specific relationship between chickenpox and

the complications which were associated with it, a comparative study was made of some of the other infectious diseases for which patients were treated in the hospital during the same five-year period. The diseases so analyzed were diphtheria, scarlet fever, measles and pertussis. The contrasting frequency of the more common complications among these diseases is shown in table 1.

It is evident from table 1 that fewer complications occur after varicella than after any of the other diseases studied. It should be noted that abscess developed with almost equal frequency in all the diseases studied. In calculating the incidence of lymphadenitis, the initial

TABLE 1.—*Frequency of Common Complications in Various Infectious Diseases*

	Varicella	Scarlet Fever	Measles	Diphtheria	Pertussis
Total number of cases	2,534	5,433	5,962	2,758	1,189
Complications	Percentage	Percentage	Percentage	Percentage	Percentage
Otitis media	1.4	11.0	23.0	5.6	14.0
Abscess	0.9	1.0	0.7	1.1	1.5
Pneumonia	0.8	1.5	12.0	4.1	19.0
Lymphadenitis	0.6	10.0	2.7	1.5	1.4
Septicemia	0.5	0.3	0.2	0.1	0.0
Mastoiditis	0.1	2.6	2.9	0.7	0.2
Empyema	0.1	0.5	1.1	0.2	0.2
Nephritis	0.1	0.6	(2 cases)	0.5	0.1
Sinusitis	0.0	2.0	0.1	0.2	0.0
Arthritis	0.0	1.9	0.1	0.2	0.1

TABLE 2.—*Incidence of Otitis Media Followed by Mastoiditis*

Disease	Total Number of Cases	Otitis Media	Mastoiditis	Percentage of Otitis Media
Varicella	2,534	37	4	10.0
Scarlet fever	5,433	603	145	24.0
Measles	5,962	1,374	174	12.0
Diphtheria	2,758	156	20	12.0
Pertussis	1,189	167	3	1.1

enlargements of the cervical nodes occurring with the pharyngitis of scarlet fever and the membrane of diphtheria were not considered; only the instances of late adenopathy are listed. Although the patients with varicella showed the fewest cases of adenitis, it is our impression that they had the greatest number of cases of adenopathy with suppuration—even a greater number than occurred in patients with scarlet fever.

Otitis media seemed more benign in patients with varicella than in those with the other diseases, as measured by the low incidence of mastoiditis. Only in patients with pertussis was there a smaller percentage of cases of mastoiditis following otitis.

In table 2 is presented the percentage of cases of otitis followed by mastoiditis in the patients with the different diseases.

Empyema occurred as a sequel to pneumonia in a greater proportion of cases of varicella than of any of the other diseases with the exception of scarlet fever, as is shown in table 3.

The most striking finding was the amazing fact that the highest incidence of septicemia was in the cases of varicella—the incidence being even higher than in the cases of scarlet fever. This is no doubt due to two factors: first, the fairly common occurrence of such pyogenic complications as abscess and cellulitis, and, second, the presence of a streptococcus as the chief offending organism.

Although the exact figures are not available it was evident on analysis that the highest incidence of cellulitis, erysipelas and gangrene occurred in the cases of varicella. Arthritis, whether serous or suppurative, did not occur with chickenpox.

There was no definite seasonal incidence of complications, nor on more minute examination was a seasonal incidence found for any of the separate complications.

The frequency of complications at different ages parallels the incidence of the disease. With few exceptions the occurrence of individual

TABLE 3.—*Incidence of Empyema as Sequel*

Disease	Total Number of Cases	Cases of Pneumonia	Number of Cases of Empyema	Percentage of Cases of Pneumonia
Varicella	2,584	21	3	14.0
Scarlet fever	5,433	82	30	36.0
Measles	5,962	721	67	9.0
Diphtheria	2,758	114	8	7.0
Pertussis	1,189	231	3	1.0

complications was not materially affected by the age of the patient. Pneumonia occurred chiefly in younger children, especially in those under 2 years; appendicitis occurred in older children, between 6 and 14 years, and herpes zoster occurred in adults.

SEX INCIDENCE

Seventy-nine males and 54 females suffered from complications after varicella.

BACTERIOLOGY

A more detailed presentation of each complication is reserved for other reports. The bacteriologic findings in the various complications were as follows:

Complication	Causative Organisms
Erysipelas	Streptococcus haemolyticus in all cases
Cellulitis	Streptococcus haemolyticus in all cases
Septicemia	Streptococcus haemolyticus in all cases but one with a Pneumococcus group IV (Avery)
Pneumonia	Almost invariably a streptococcus; Str. haemolyticus more frequently than Streptococcus viridans
Empyema	Almost invariably a streptococcus, usually Str. haemolyticus; Pneumococcus type XIV in one case
Abscess and suppurative lymphadenitis	Str. haemolyticus and Staphylococcus aureus with about equal frequency
Otitis media	Staph. aureus, Str. haemolyticus, Staph. albus, Str. viridans and Pneumococcus, in order of frequency
Gangrene	Various organisms, including Str. haemolyticus, Staph. aureus, Staph. albus and Bacillus coli

MORTALITY

The mortality in the various diseases is shown in table 4. In cases of varicella death was always due to a complication. Of the cases of varicella ending fatally, septicemia was the complication in 7, associated with cellulitis in 2 cases, and with endocarditis, meningitis, gangrene and pneumonia in 1 case each. In 2 cases encephalitis caused death and empyema and intestinal intoxication, in 1 case each.

TABLE 4.—*Mortality in Various Infectious Diseases*

Disease	Deaths	Percentage	Total No. of Cases
Varicella	11	0.4	2,534
Scarlet fever	82	1.5	5,433
Measles	161	2.7	5,962
Diphtheria	145	5.2	2,758
Pertussis	82	6.8	1,189

CONCLUSIONS

Varicella is not as innocuous as it is usually considered to be.

Of 2,534 cases studied over a five year period, complications occurred in 5.2 per cent.

The usual complications are such pyogenic conditions as otitis media, abscess, suppurative lymphadenitis, cellulitis and erysipelas.

The offending organism usually associated with the complications is a hemolytic streptococcus (Streptococcus beta).

Septicemia occurred in 0.5 of the cases, a percentage higher than that for four other contagious diseases studied.

The total mortality of the entire series of patients with varicella was 0.4 per cent.

COMPLICATIONS OF VARICELLA

II. SURFACE COMPLICATIONS

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Among 2,534 patients treated for varicella at the Willard Parker Hospital over a five year period between Jan. 1, 1929, and Dec. 31, 1933, 133, or 5.2 per cent, as previously reported,[1] suffered complications. Of these, 76, or 57 per cent, suffered from infection of the surface of the body involving the skin, mucosa, subcutaneous tissues or glands. It is thus evident that infections of the surface of the body constitute one of the major considerations in the care of patients with chickenpox.

Listed in the order of frequency, the surface complications observed were:

	Patients
Cutaneous abscess	24
Lymphadenitis	16
Cellulitis of skin and subcutaneous tissues	16
Erysipelas	7
Gangrene of skin and subcutaneous tissues	4
Impetigo	4
Paronychia	3
Conjunctivitis	3
Balanitis	2
Hordeolum	1
Blepharitis	1
Stomatitis	1
Parotitis	1

ERYSIPELAS

Erysipelas occurred in 7 cases. In 6 it appeared surrounding a varicella lesion, evidently arising as an infection of the lesion. In the other case, an abscess about a pock was incised, after which erysipelas developed about the wound. The parts of the body involved were: the face, 5 patients; the scalp, 4; the extremities, 2, and the trunk, 1. The erysipelas set in early in the illness, between the second and the ninth day, except in the case in which erysipelas followed the incision

1. Bullowa, J. G. M., and Wishik, Samuel M.: Complications of Varicella, Am. J. Dis. Child., this issue, page 923.

of an abscess. In that case, erysipelas appeared on the twentieth day of illness. Most of the patients had a fairly heavy varicella rash. The erysipelas was usually associated with a temperature of 104 F. or higher, which persisted for from three to ten days, with no definite relation to serum therapy.

In 2 cases there were further complications; suppurative lymphadenitis in 1, and local breakdown of the involved area with the formation of an abscess in the other. In the latter the lesions continued to spread despite the administration of serum and transfusions; an infection in the blood stream resulted, and the patient died fifteen days after the onset of erysipelas. This was the only death among the 7 patients.

Bacteriology.—Hemolytic streptococci were isolated from the infected surfaces, from the suppurative lesions and, in the case in which death occurred, from the blood stream.

CELLULITIS

Sixteen patients had cellulitis of the skin and deeper tissues, which differed from erysipelas in appearance, margination and mode of spread. The infection developed about a small locally inflamed varicella lesion in all but 2 cases. In these 2 cellulitis appeared about an abscess. All parts of the body were attacked almost indiscriminately. Cellulitis invariably developed in the first week of illness, most often before the fourth day after the appearance of the chickenpox rash, which was usually heavy.

The deep-seated infection invaded the subcutis as well as the surface of the skin and suppurated in all but 1 case. In that case the infection was mild, subsiding spontaneously in one day. In the 15 cases in which the condition progressed to suppuration, spontaneous drainage occurred in 4 from two to seven days after the onset of cellulitis. Drainage was established through a sinus formed by the scab's dropping off the central pock about which the infection had set in. In 4 cases, within from two to six days central sloughing of the tissue rather than formation of a sinus provided a mode of outlet. In the remaining 7, drainage was instituted by incision within from three to fourteen days.

Cellulitis usually subsided when signs of localization and the formation of an abscess appeared. If cellulitis continues to spread despite the institution of drainge, the prognosis is bad. The 3 patients in whom localization, incision and drainage of pus failed to halt the extension of the inflammatory process died. Such infections were uniformly associated with septicemia.

The temperature remained above 103 F., except in the mildest cases, until cellulitis subsided or until shortly after drainage was established.

The temperature often reached 105 or 106 F. It was above 104 F. in the 3 patients who died.

The abscesses which were drained by incision cleared up most quickly, usually in about a week. Drainage through a sinus formed by the removal of a varicella scab was less satisfactory. The pus was repeatedly dammed back and drained intermittently for from two to three weeks. The abscesses which drained by sloughing were the slowest to heal, it usually being a month or more before the discharge stopped. In 3 cases with this form of drainage the slough reached the proportion of gangrene, terminating fatally in 1.

Other serious complications frequently occurred in association with, and usually following, cellulitis. These included: septicemia, 6 cases; pneumonia, 2; osteomyelitis, 2; gangrene, 3; otitis media, 2 and nephritis, 1.

Bacteriology.—A hemolytic streptococcus was the offender when organisms were isolated from the skin surface, the abscess or the blood stream.

ABSCESS

The largest group in the series consisted of 24 patients in whom cutaneous abscesses developed without previous cellulitis. The abscesses occurred in mild as well as in severe cases of chickenpox. They were located on all parts of the body, especially on the scalp, on the face, in the submental region and on the neck. They appeared at almost any period during the presence of the rash, even as late as the fifteenth day. The abscess nearly always formed about a pock. In 1 case it developed at the site of a hypodermoclysis given to a septic patient. The death of this patient was the only one in this series and was not attributed to the incidental abscess.

Abscesses occurred in 5 patients previously suffering from complications: septicemia, in 1; otitis media, in 1; empyema, in 1, and pneumonia, in 2. The abscesses were rarely followed by a serious complication. Except in the cases of the 2 patients with cellulitis and the 1 with erysipelas, recovery was uneventful. The temperature usually remained below 103 F., reaching 104 F. in only 4 instances.

In all but 1 case the abscess drained within a week after its appearance; in 6 spontaneously and in 17 others by incision. Of the 22 patients who recovered after drainage was established, the abscesses ceased draining in 9 within a week, in 8 within two weeks, in 3 within three weeks and in 2 within a month.

Bacteriology.—A hemolytic streptococcus was the most common organism. Hemolytic staphylococcus (Staphylococcus aureus) was seen less frequently. Streptococcus viridans was isolated in one case.

LYMPHADENITIS

Lymph nodes became inflamed in 16 patients. Cervical nodes were involved in 8, inguinal in 3, axillary and postauricular in 2 and preauricular and submaxillary each in 1 patient. Some of the infections of the cervical nodes were no doubt secondary to infection in the throat. Preauricular lymphadenitis followed an abscess of the face in 1 instance, and an inguinal swelling followed cellulitis of the penis and scrotum in another. In the remainder of the cases, there were no demonstrable antecedent infections to account for involvement of the lymph nodes. Probably a relatively insignificant transient infection of a varicella lesion constituted the focus from which the nodes were invaded.

Lymphadenitis occurred at any period of the rash, from the appearance of the early vesicle to that of the dry scab. It caused variable elevation of the temperature usually above 103 F., but the fever readily subsided once softening had developed and even before drainage was instituted. Suppuration occurred in all but 2 cases. The nodes broke down early and responded well to incision and drainage. The prognosis was uniformly good. There was no local extension after incision, and secondary distant infections were seldom encountered. There were no deaths in the series, despite pneumonia in 1 patient and septicemia in another.

Bacteriology.—A hemolytic streptococcus and Staph. aureus were the offending organisms.

GANGRENE

Cutaneous gangrene occurred in 4 patients, 3 of whom were mentioned in the group with cellulitis. In all cases gangrene developed during the first week of varicella, but in 1 new areas of necrosis continued to appear as late as the twenty-fifth day. Some of the lesions were probably related to the type of subcutaneous gangrene described by Meleney.[2]

CASE 1.—A 2 year old child had septicemia associated with extensive cellulitis of the neck, one shoulder and the wall of the chest. Incisions caused a discharge of pus from several fluctuant areas. Nevertheless, cellulitis continued to spread peripherally, and the central area became necrotic. The necrosis reached the proportions of gangrene of the shoulder and anterior wall of the chest, extending through the deep tissues to the muscle. The temperature was maintained at a plateau level above 104 F., and the patient died after five days. Hypostatic pneumonia was present terminally. A hemolytic streptococcus was isolated from the gangrenous tissues as well as from the blood stream.

CASE 2.—In a 1 year old girl, on the third day of illness with varicella, cellulitis of the shoulder region was ushered in by convulsions. The next day the child was

2. Meleney, Frank L.: Hemolytic Streptococcus Gangrene, Arch. Surg. **9**:317 (Sept.) 1924.

desperately ill, evidently septic, and cellulitis spread to the front and back of the wall of the chest. On the sixth day of illness, central necrosis appeared, and two days later a deep slough, 6 by 3 inches (182.86 by 91.4 cm.), separated from the shoulder region. Four days later a large portion of the trapezius muscle was exposed. Between the fourth and the twenty-fifth day of illness, new foci of infection continued to appear in scattered parts of the body surface, including the opposite shoulder, axillae, forearms, fingers, groins, thighs, legs, toes and scalp. Some drained spontaneously, and others required incision, but an area behind one ear and three lesions higher on the scalp became definitely necrotic and gangrenous. The child's temperature rose to 106 F. daily during the first week and up to 103 during the second week, and fluctuated irregularly below 101 thereafter. When the patient was discharged from the hospital fifty days after admission, all the wounds were free from drainage except on one finger, where osteomyelitis of a phalanx had developed.

CASE 3.—In a 20 year old man there developed cellulitis of the scrotum four days after the onset of chickenpox. Three days later sloughing began, accompanied by extensive undermining of the adjacent areas. The gangrene continued to spread until the scrotal sac was completely denuded, leaving a surface of glistening white, deep fascia. The temperature remained below 102 F. throughout. When the patient was discharged from the hospital a month later there was no sign of regeneration of the skin. Stapylococcus aureus and Bacillus coli were isolated from the edges of the wound.

CASE 4.—The fourth case differed from the preceding ones in that the gangrene was not preceded by cellulitis. A 3 year old boy had a mild case of varicella and played about the house until the ninth day of illness, when he first had difficulty in walking. Three days later the fingers of the left hand displayed a purplish discoloration, followed the next day by similar involvement of the right foot and lower part of the leg. When the patient was admitted to the hospital on the fourteenth day of illness, there were dry, black gangrenous patches involving all the fingers and most of the rest of the left hand, the dorsum of the right foot, the lower third of the anterior surface of the right leg and an area below the left knee. Blebs appeared on the surface of the lesions, and the areas extended slightly the next day. Then demarcation set in. The fingers became mummified. The two distal phalanges of each finger and of one toe and the skin of the leg and foot separated within a month after the complication first appeared. At no time did the patient seem very ill, toxemic or prostrated. His temperature was 102 F. during the first week in the hospital. Cultures from skin blebs and from the gangrenous areas were uniformly sterile.

CONJUNCTIVITIS

Many patients suffering from chickenpox have conjunctival congestion and excessive lacrimation, but only 3 in this series had severe purulent conjunctivitis. This complication occurred on the second or third day after the appearance of a heavy generalized varicella rash. Both eyes were involved in 1 patient. Conjunctivitis was the only complication in 2 patients, but in the third it was associated with other infections, including blepharitis and balanitis. The condition cleared up readily within from four to six days and left no sequelae. A gram-positive coccus was isolated from the secretion from 1 patient; no organisms were found in the others.

OTHER COMPLICATIONS

The other complications listed at the beginning of the paper were of little importance and require no discussion. There was no suppuration in the case of paratitis.

CONCLUSIONS AND SUMMARY

Of the patients with varicella suffering from complications, 57 per cent had infections of the skin, surface mucosa and lymph glands.

The complications appearing most frequently were abscess, suppurative lymphadenitis, cellulitis and erysipelas.

The apparent portal of entry is almost invariably a pock.

The hemolytic streptococcus is the sole cause of cellulitis and erysipelas and the chief offender in cases of abscess and suppurative lymphadenitis.

Cellulitis almost always suppurates about apparent portals of entry. It is one of the most dangerous of the more common complications of varicella.

Abscess usually causes little trouble, but requires drainage.

Infected lymph nodes almost always break down and drain externally. Recovery is uneventful.

Cutaneous gangrene may follow severe cellulitis or may occur independently.

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EOSINOPHILIA IN SCARLET FEVER

I. AS A DIAGNOSTIC AID

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The diagnosis of the acute exanthems and other acute infectious and contagious diseases of childhood may at times be simple and obvious. In some cases, however, one's diagnostic ability is taxed to the utmost, and any diagnostic aid, such as a characteristic blood picture, is welcome. Thus the leukocytosis and relative lymphocytosis present in pertussis are frequently important factors in establishing the presence of that disease. The leukopenia of rubeola is also well known. The eosinophilia of scarlet fever, however, seems to be a greatly neglected phenomenon. Not only is there widespread ignorance of the presence of eosinophilia in scarlet fever, but its application as a diagnostic aid seems to be practically nonexistent. Doubtless this is due in part to the relative paucity of literature on the subject. Pediatric textbooks in general devote a scant line or two to the subject and vary considerably in the information offered.

Only a few meager reports [1] on this phenomenon have appeared in the English literature since Bowie's [2] early work. Bowie tabulated forty-three cases of "simple" scarlet fever, twenty-three cases of the "anginose" type and four fatal cases in which a single eosinophil count was made. In seven of eleven simple cases in which the eosinophil count was determined some time during the first week of illness the eosinophil count was over 4 per cent. In only two of the eleven anginose cases in which the determination was made during the first eight days of the disease was there an elevated eosinophil count. In all the fatal cases there was a subnormal count. Bowie concluded that in simple or mild cases the eosinophil count reaches its maximum some time during the first week of the disease and then declines, and that in moderately severe cases the count does not attain its maximum until somewhat later in the disease.

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1. (*a*) Bunting, C. H., and Thewlis, E.: Leukocytic Reactions in Smallpox, Chickenpox, Scarlet Fever, Measles and Mumps, Arch. Path. **1**:189 (Feb.) 1926. (*b*) Lindsay, J. W.; Rice, E. C., and Selinger, M. A.: The Blood in Scarlet Fever, Virginia M. Monthly **53**:709 (Feb.) 1927

2. Bowie, J. M.: The Leukocytosis of Scarlet Fever and Its Complications, J. Path. & Bact. **8**:802, 1902.

Somewhat more attention has been paid to this phenomenon in the German literature.[3] Von Ambrus found the eosinophil count usually to range from 5 to 7 per cent from the fourth to the sixth day of the disease and then gradually to decline. The increased eosinophil count might be found as early as the second day in mild cases. In severe cases eosinophils were practically absent from the circulating blood. Bix found the percentage of eosinophils to be definitely elevated from the fourth to the seventh day of the disease, usually attaining a maximum about the sixth day.

There is a single French contribution by Markovitch and Guératovitch,[4] who reported that in mild cases the eosinophil count is elevated throughout the acute stage of the disease and usually attains a maximum of 12 per cent or more of the total leukocyte count. About the twelfth day of the illness the percentage of eosinophils begins to decline, reaching a normal level about the twenty-fifth day of the disease. In severe cases the eosinophil count is low during the acute phase and rises with general amelioration of the patient's condition.

However, from none of these reports save that of Bowie, in which only twenty-six cases seen in the early stage are listed, can one ascertain how helpful an examination of the blood for eosinophilia may be as an early diagnostic aid, for the percentage of cases in which the phenomenon was exhibited is not given. The present study was undertaken primarily from the standpoint of the physician in an effort to determine how helpful the eosinophil count may be in the early diagnosis of scarlet fever. However, the number of highly interesting questions which have arisen has caused a continuation of the work, of which this is the first report.

METHODS AND MATERIAL

An eosinophil count was made in the cases of one hundred patients with scarlet fever who were admitted to the South Department of the Boston City Hospital. These cases were not absolutely consecutive, as the cases of patients who presented a late stage, cases in which there were complications and cases in which there were cross-infections were omitted, for obvious reasons. The count was made on the day of, or on the day following, admission. My impression is that on the average the test was made from about twenty-four to thirty-six hours after the appearance of the rash. All the counts were made at approximately the same time of day—3 p. m. Blood smears were made by the slide method and stained with

3. von Winterfield, H. K., and Hahne, E.: Ueber die differential diagnostische Verwendbarkeit des leukocytären Blutbildes bei Mäsern und Scharlach, Klin. Wchnschr. **2**:1977 (Oct. 22) 1923. von Ambrus, J.: Ueber das Blutbild beim Scharlach, Jahrb. f. Kinderh. **101**:81 (Sept.) 1923. Bix, H.: Hämatologische Studien bei Scharlach, Med. Klin. **21**:1689 (Nov. 6) and 1728 (Nov. 13) 1925.

4. Markovitch, V., and Guératovitch, M.: L'éosinophilie au cours de la scarlatine, Presse méd. **33**:205 (Feb. 14) 1925.

Wright's stain. Three hundred white blood cells (100 in each of three portions of the slide) were counted in determining the percentage of eosinophils. The definition of the upper limit of the normal eosinophil count is difficult, especially in children. Schilling designated from 2 to 4 per cent as the normal percentage of eosinophils and termed values over 4 per cent as elevated. I believe that 4 per cent may be taken as the maximal normal limit; all counts over 4 per cent are therefore termed elevated.

RESULTS

The individual results are listed in table 1 and summarized in tables 2, 3 and 4.

It may be seen that a single examination of the blood revealed an elevated eosinophil count in 46 per cent of all the cases in the early stages of the disease. What percentage of patients ultimately show an elevated eosinophil count does not seem to be recorded definitely in the literature. Lindsay, Rice and Selinger [1b] reported eosinophilia at some time in 50 per cent of their cases. As will be seen in a later report,[5] this figure is much too low. The enormous eosinophil counts recorded by one or two authors were not found, as a rule, in my series. Most of the elevated counts ranged from 5 to 8 per cent. The highest count recorded was 17 per cent, although of course these counts were not, save fortuitously, the maximal ones attained.

If one analyzes further in what type of case eosinophilia is most likely to appear in the early stages of the disease, one sees in table 2 that in 60 per cent of the mild cases there was an elevated eosinophil count, while in only 18.2 per cent of the moderate cases and in none of the severe cases did the patient display that phenomenon. Viewed from a slightly different angle, it may be seen that forty-two of the forty-six patients (or 91.3 per cent) displaying an elevated eosinophil count in the early stages of the disease had a mild form of the disease. Emphasis should be placed also on the type of rash displayed. Thus, in the early stages, 62.1 per cent of the patients exhibiting a slight or a very slight rash had an elevated eosinophil count while only 31 per cent of those with a moderate rash and 7.7 per cent of those with a bright or intense rash had an elevated eosinophil count. The relationship between the degree of constitutional symptoms, as typified by the temperature, and the eosinophil count is similar to the relation between the severity of the case and the eosinophil count.

It may be readily seen that the type of case in which an elevated eosinophil count is most likely to be seen in an early stage of the disease, i. e., from the third to the fifth day, is the mild case with only a slight rash and mild constitutional symptoms.

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5. Friedman, S.: Eosinophilia in Scarlet Fever: II. General Considerations, Am. J. Dis. Child., to be published.

TABLE 1.—*Individual Eosinophil Counts in One Hundred Cases of Scarlet Fever*

Case	Severity	Day of Disease	Temperature, F.	Eosinophil Count	Type of Rash
1	Moderate	5	101.0	0.3	Slight
2	Mild	4	98.6	4.7*	Slight
3	Mild	6	98.6	1.3	Very slight
4	Moderate	5	101.6	3.7	Very slight
5	Severe	2	103.0	0.0	Bright
6	Mild	6	98.6	7.0*	Very slight
7	Mild	5	98.6	5.0*	Slight
8	Mild	2	99.6	7.0*	Moderate
9	Moderate	3	102.0	0.0	Intense
10	Mild	3	101.0	3.7	Moderate
11	Mild	4	98.6	6.0*	Moderate
12	Mild	3	99.6	7.0*	Moderate
13	Mild	4	100.6	7.3*	Moderate
14	Mild	5	98.6	4.3*	Very slight
15	Mild	3	98.6	5.0*	Very slight
16	Mild	3	98.6	4.3*	Very slight
17	Severe	5	102.0	0.0	Moderate
18	Mild	4	98.6	1.0	Slight
19	Mild	3	100.0	4.7*	Slight
20	Mild	4	98.6	6.0*	Slight
21	Mild	4	98.6	2.0	Very slight
22	Mild	4	98.6	8.0*	Slight
23	Mild	5	98.6	8.0*	Very slight
24	Moderate	3	101.0	5.7*	Moderate
25	Mild	4	100.6	4.0	Moderate
26	Severe	3	103.0	1.7	Bright
27	Mild	4	99.4	6.7*	Very slight
28	Severe	2	103.0	0.7	Moderate
29	Mild	5	98.6	8.0*	Very slight
30	Moderate	3	103.0	1.7	Intense
31	Severe	4	103.0	0.7	Intense
32	Moderate	4	101.0	1.3	Slight
33	Mild	6	98.6	5.0*	Slight
34	Moderate	4	101.0	2.0	Moderate
35	Moderate	3	101.0	3.3	Moderate
36	Mild	4	98.6	8.7*	Very slight
37	Mild	4	98.6	4.7*	Slight
38	Mild	5	98.6	3.0	Slight
39	Severe	5	100.0	1.7	Bright
40	Mild	3	98.6	4.3*	Very slight
41	Moderate	2	101.0	2.7	Bright
42	Moderate	3	100.6	3.0	Moderate
43	Moderate	4	101.0	3.7	Moderate
44	Mild	5	98.6	1.7	Moderate
45	Mild	4	98.6	2.0	Very slight
46	Moderate	5	98.6	7.0*	Moderate
47	Mild	4	98.6	8.7*	Slight
48	Moderate	3	103.0	3.7	Moderate
49	Moderate	3	103.0	2.7	Intense
50	Mild	4	99.8	7.7*	Very slight
51	Mild	4	99.6	8.7*	Slight
52	Moderate	4	101.0	3.0	Bright
53	Mild	5	98.6	2.3	Very slight
54	Mild	3	98.6	4.0	Slight
55	Mild	4	99.6	2.0	Slight
56	Mild	4	100.0	14.0*	Very slight
57	Moderate	3	101.0	0.3	Moderate
58	Mild	5	99.6	2.0	Slight
59	Mild	4	98.6	5.7*	Slight
60	Moderate	5	101.0	5.0*	Moderate
61	Mild	5	100.0	10.7*	Slight
62	Mild	3	98.6	8.0*	Very slight
63	Mild	4	100.6	3.7	Moderate
64	Moderate	4	102.0	1.3	Slight
65	Mild	5	100.6	1.3	Very slight
66	Mild	2	100.0	2.0	Slight
67	Mild	4	98.6	5.3*	Slight
68	Severe	4	101.0	3.3	Intense
69	Moderate	4	101.0	2.0	Slight
70	Mild	5	98.6	6.0*	Slight
71	Mild	2	100.0	2.0	Moderate
72	Mild	3	98.6	3.0	Slight
73	Mild	3	100.4	2.0	Moderate
74	Mild	7	98.6	5.7*	Very slight
75	Mild	4	98.6	8.0*	Slight

* This count was elevated beyond the maximal limit of normal.

TABLE 1.—*Individual Eosinophil Counts in One Hundred Cases of Scarlet Fever —Continued*

Case	Severity	Day of Disease	Temperature, F.	Eosinophil Count	Type of Rash
76	Moderate	4	100.0	4.7*	Moderate
77	Moderate	5	101.0	1.0	Very slight
78	Mild	3	100.0	3.0	Moderate
79	Mild	5	98.6	5.0*	Very slight
80	Mild	2	98.6	2.0	Bright
81	Mild	2	98.6	4.3*	Bright
82	Mild	4	98.6	9.0*	Slight
83	Mild	4	100.0	3.3	Slight
84	Mild	6	98.6	4.0	Very slight
85	Mild	4	100.0	4.7*	Very slight
86	Moderate	2	100.4	3.0	Slight
87	Mild	3	98.6	9.7*	Very slight
88	Severe	3	103.0	0.0	Intense
89	Mild	4	98.6	17.0*	Very slight
90	Mild	2	98.6	5.3*	Very slight
91	Mild (recurrent)	2	98.6	4.7*	Very slight
92	Mild	5	98.6	1.3	Moderate
93	Mild	4	98.6	6.3*	Slight
94	Mild	2	99.4	1.7	Moderate
95	Mild	2	100.0	0.7	Moderate
96	Mild	4	98.6	6.7*	Slight
97	Mild	3	98.6	2.0	Moderate
98	Mild	2	100.2	2.7	Slight
99	Moderate	2	100.4	0.0	Slight
100	Mild	3	98.6	4.7*	Moderate

TABLE 2.—*Comparison of the Incidence of Eosinophilia and the Severity of the Condition*

Severity	Total Number in Group	Number with Eosinophilia	Percentage of Group with Eosinophilia
Mild	70	42	60.0
Moderate	22	4	18.2
Severe	8	0	0.0

TABLE 3.—*Comparison of the Incidence of Eosinophilia and the Type of Rash*

Type of Rash	Total Number in Group	Number with Eosinophilia	Percentage of Group with Eosinophilia
Very slight or slight	58	36	62.1
Moderate	29	9	31.0
Bright or intense	13	1	7.7

TABLE 4.—*Comparison of the Incidence of Eosinophilia and the Temperature at the Time of the Blood Count*

Temperature, F.	Total Number in Group	Number with Eosinophilia	Percentage of Group with Eosinophilia
Normal	46	33	71.7
99.2 to 101	42	13	30.9
Over 101	12	0	0.0

COMMENT

It seems fortunate that it is mild scarlet fever with a slight, barely perceptible rash in which eosinophilia is most likely to be present in the early stages of the disease. Typical scarlet fever of moderate severity with fairly pronounced scarlatiniform eruption offers very little difficulty in diagnosis. It is the mild form in which there are practically no pathologic changes in the throat and only a slight rash, frequently seen only in the folds of the skin or in the groins, which taxes one's diagnostic ability. Because of the relatively mild character of the epidemics of recent years, one sees more and more of these cases rather than those of the severe or moderately severe type. In mild cases, any diagnostic aid is to be welcomed, and an examination of the blood for eosinophilia should become a more accepted and general laboratory procedure. If the examination for eosinophilia gives negative results on one occasion it should be repeated once or twice on succeeding days. The only other condition in which eosinophilia is present that need be differentiated is serum sickness, and this is usually readily ruled out by the history.

The presence of eosinophilia in scarlet fever is, then, a phenomenon of practical importance and interest. However, of even greater, although possibly more theoretical, interest is the nature or explanation of the presence of this phenomenon. This will be discussed in succeeding communications.

SUMMARY

An eosinophil count was made in one hundred cases of scarlet fever in the early stages of the disease. In 46 per cent of the cases eosinophilia was demonstrated in a single count.

Eosinophilia is most likely to be present in the early stages of the disease in the mild cases in which there are mild constitutional symptoms and a mild rash. The incidence of eosinophilia in such cases was from 60 to 70 per cent as compared with 46 per cent in all cases of the disease. It is in the mild type of case that frequently there is difficulty in making the diagnosis. The use of the presence of an elevated eosinophil count as an aid to diagnosis is recommended.

RELATION BETWEEN INFECTION OF THE UPPER RESPIRATORY TRACT AND GASTRO-INTESTINAL INFECTION IN INFANTS

WITH SPECIAL REFERENCE TO THE RÔLE OF BACILLUS MORGANI I

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During the early part of July 1933 an epidemic of infection of the upper respiratory tract associated with diarrhea broke out in one of the wards of the Home for Hebrew Infants. There had been no infection in the ward for the previous eight weeks. There were in the ward twenty-three children, all under 1 year of age, each in a separate, completely enclosed cubicle. Each compartment opened on a common porch on which the children spent the better part of the day. No change had been made in the nursing staff or in the aseptic technic preceding the epidemic.

On June 26 a poorly nourished child 5 months old was admitted to the ward. The examination on admission revealed no signs of infection. For the first two days the child appeared to be thriving, but on the third day it had three loose, foul-smelling stools. During the next eight days there were five or six loose, greenish-yellow stools with much mucus but no blood. The day after the onset of the diarrhea the child's throat was moderately congested. Both ear drums were red, lusterless and slightly bulging. The child took its food poorly and vomited once daily for the first three days. The temperature did not rise above 99 F. at any time during the illness. The left ear drum opened spontaneously six days after the onset of the illness. The child lost 7 ounces (198 Gm.) during the first three days of the illness and did not regain the weight shown on admission, 9 pounds and 10 ounces (4,365.8 Gm.), until eleven days after the onset.

Five additional cases developed during the next two weeks. The clinical picture was almost identical in each. The onset was marked by an increase in the number of stools. The normal number of one or two daily was increased to three or four loose, yellowish-green evacuations. As the disease progressed the stools became more frequent, with from five to seven moderate-sized movements occurring daily. The stools were loose to watery and green and contained much mucus but no blood. All the affected children had red throats and signs of disease

From the Home for Hebrew Infants, service of Dr. Sidney V. Haas, and the Laboratories and Outpatient Department of Lebanon Hospital.

of the middle ear. The latter varied from lusterless drums with a leash of congested vessels to marked bulging with spontaneous perforation. In one case myringotomy was performed and pus was obtained. In no case did the temperature go above 100 F. There was an invariable rapid loss of weight ranging between 7 ounces and 1 pound (453 Gm.) in the first three or four days of the illness. Three of the six children vomited once or twice daily for the first two days of the disease. The vomiting was not severe and made up a minor part of the clinical picture. Anorexia was a constant symptom. Children whose appetites had previously been excellent for a long period suddenly refused most of their usual feedings.

The time elapsed from the onset of abnormal stools and the beginning of loss of weight to the return to normal, as evidenced by normal stools and attainment of the weight shown before the illness, was between eight and ten days.

Five of the infants were treated solely by the use of protein milk with 3 per cent dextrimaltose. The infant whose ear drum was opened began to improve the next day, so no change in the feeding formula was made.

Since the six children were all suffering from a gastro-intestinal disturbance accompanied by definite evidence of disease of the upper respiratory tract, and since the population of the ward was peculiarly well controlled, it was thought that this would be a favorable opportunity to investigate the intestinal flora in an effort to throw some light on a controversial subject.

METHOD OF INVESTIGATION

A uniform technic was followed in all cases. Material for study was obtained by introducing a sterile swab into the rectum and twirling it gently to obtain a fair sample. This was immediately emulsified in a tube of glucose broth and plates were streaked from this medium within the next hour. Three plates of Levine's eosin-methylene blue agar (prepared from the Difco desiccated product) were used in each case. With a little practice uniform plates free from spreaders and containing between 150 and 300 well separated colonies were obtained.

The plates were incubated for twenty-four hours at 37.5 C. Suspicious colonies were transferred to 2 per cent lactose peptone water (brilliant cresyl purple indicator) and incubated for at least five days in order to eliminate the late lactose fermenters. Not all suspicious colonies were picked, except when their number was less than 10. In all other cases at least 3 similar-looking colonies from every batch of plates were transferred to the lactose peptone water.

In the routine examination the following sugars were used: dextrose, lactose, saccharose, mannitol, levulose, galactose, maltose, arabinose, dulcite, inosite and xylose. All organisms were grown on litmus milk and on gelatin for one week. The indole test, using the Ehrlich reagent, was done on a three day growth of the organisms in peptone water.

If no nonlactose fermenters were recovered from the first set of plates, another sample of stool was plated three days later. If this showed no nonlactose ferment-

ers two additional series of plates were inoculated at three day intervals before this group of organisms was considered absent.

The organisms recovered were classified according to the system outlined by Bergey,[1] except that Bacillus paracoli was classified according to the system of Castellani and Chalmers.[2] In table 1 are shown the nonlactose-fermenting organisms recovered from the intestines of the sick children.

TABLE 1.—*The Nonlactose-Fermenting Organisms Recovered from the Intestines of Sick Infants*

Infants	Age, Months	Organisms Recovered	
		First Plating	Subsequent Platings
S. D.	5	B. Morgani I	
D. V.	5	B. paracoli	B. Morgani I
R. B.	5	B. Morgani I	
A. K.	4½	B. paracoli	B. paracoli
R. H.	5½	B. Morgani I	
R. L.	4½	B. Morgani I	

TABLE 2.—*The Nonlactose-Fermenting Organisms Recovered from the Intestines of Well Infants*

Infant	Organisms Recovered	
	First Plating	Subsequent Platings
L. M.	0	B. Morgani I
M. F.	0	B. Morgani I
D. N.	B. Morgani I, B. paracoli	
B. G.	0	B. Morgani I, B. paracoli
N. F.	0	B. Morgani I
R. v W.	0	B. Morgani I
H. B.	0	0
C. L.	0	B. Morgani I
E. A.	0	B. Morgani I
G. R.	0	B. Morgani I, P. asiaticus
L. F.	0	B. Morgani I
B. S.	P. asiaticus	P. asiaticus
J. L.	B. Morgani I	
B. L.	B. paracoli	0
J. R.	B. Morgani I	
A. N.	B. Morgani I	
I. S.	B. Morgani I	
W. B.	0	0
C. S.	P. asiaticus	B. paracoli
R. F.	P. asiaticus, B. Morgani I	0
R. G.	P. asiaticus	B. paracoli

The seventeen remaining children in the ward, all of whom were well, and four children who were admitted after the epidemic was over were examined for the presence of nonlactose fermenters in the stool in the same manner as were the sick children. The results are set forth in table 2. No child was younger than 3 months and none was older than 1 year.

1. Bergey, D. H.: Manual of Determinative Bacteriology, Baltimore, Williams & Wilkins Company, 1923.

2. Castellani, A., and Chalmers: Ann. Inst. Pasteur **34**:616, 1920.

The prevalence of Bacillus Morgani I, Proteus asiaticus and B. paracoli in the group of well infants pointed to the possibility that these organisms might be common in the general infant population. To determine this a group of thirty-eight infants, all under 1 year of age, were chosen from the infant hygiene clinic of Lebanon Hospital. None of the infants had had diarrhea or an infection of the upper respiratory tract for at least one month prior to examination. The children came from a poor section of the Bronx where the conditions in the home, the milk, the food supply and the general hygiene were practically identical. Table 3 shows the frequency of occurrence of the nonlactose fermenters in the stools of these infants.

From the stools of eleven children nonlactose fermenters were not recovered. Stools from these children were plated only once owing to the shifting population of the clinic. Of six children specimens of whose stools originally gave negative results but from whom additional cultures could be obtained, subsequent examination gave positive results

TABLE 3.—*Occurrence of Nonlactose-Fermenting Organisms in a Group Not Hospitalized*

Organism	Alone	Associated with Other Organisms
B. Morgani I	11	3
B. paracoli	4	3
P. asiaticus	3	2
P. vulgaris	3	2

in four cases. Had the opportunity existed to reexamine specimens from the eleven in whom negative results were obtained, B. Morgani I and the other nonlactose fermenters undoubtedly would have been found in the majority.

From tables 1, 2 and 3 it is seen that while B. Morgani I was recovered from the stools of five of the sick infants, it was recovered from the stools of fifteen of the twenty-one controls in the same ward. It was recovered from the stools of fourteen of thirty-eight infants not hospitalized and undoubtedly would have been found in a higher percentage had more numerous platings been possible in the case of those whose specimens failed to show B. Morgani I at the first plating.

Blood serum from all the sick infants was tested against the homologous strain of B. Morgani I when that organism was discovered, but agglutination failed to take place in every case. Blood serum from all the infants from whose stools P. asiaticus was recovered also failed to agglutinate the homologous strain.

An agglutinating serum for two strains of B. Morgani I was made by repeated intravenous injections into rabbits of killed and living cultures isolated from the stools of the sick infants. A titer of 1:2,560

for the homologous organism was obtained. Cross-agglutination, however, did not take place in a dilution greater than 1 : 100.

All the remaining strains were tested with the two agglutinating serums, and in no case did agglutination occur in dilutions higher than 1 : 640. In most instances agglutination did not occur in dilutions higher than 1 : 160.

This conclusively proves that the organisms isolated were of different strains and that the epidemic could not have been due to a single virulent strain of B. Morgani I.

It is the purpose of this paper to show that the mere recovery of an organism from a stool of an infant with diarrhea does not prove that it is the cause of the diarrhea. Especially in the case of organisms the pathogenicity of which is doubtful or not constant, such as B. Morgani I or P. asiaticus, such a conclusion is unwarranted unless the organism is also recovered from the blood, as has been reported by Havens and Ridgway,[3] or when positive agglutination reactions against the homologous organism occur in dilutions higher than 1 : 40.

PATHOGENICITY FOR ANIMALS

Morgan and Ledingham[4] in 1909 summarized the results of four years' work on the bacteriology of summer diarrhea. Their feeding experiments showed that the organism produced death in twenty-four hours in young rats and in rabbits. The organism was recovered regularly from the spleen and occasionally from the heart's blood. Four monkeys were each fed one agar tube of a twenty-four hour culture, and all died following acute diarrhea. The strains isolated by these authors in 1907-1908 were much less virulent. Monkeys had diarrhea but did not die. The organisms fed in every case were from patients with diarrhea.

Havens and Ridgway[3] reported on a group of thirteen patients presenting clinical symptoms in common and offered evidence pointing to B. Morgani I as the etiologic agent. They injected from 0.1 to 0.5 cc. of a twenty-four hour broth culture intraperitoneally into mice and guinea-pigs. This caused death in twenty-four hours when the organism injected was from one of the authors' patients. However, seven strains recovered from normal persons were not pathogenic for mice or guinea-pigs even when as much as 1 cc. was injected intraperitoneally.

I tested the pathogenicity by intraperitoneal injection of all five strains recovered from the sick children and also of ten strains recov-

3. Havens, L. C., and Ridgway, C.: The Pathogenicity of Morgan's Bacillus: A Series of Thirteen Cases Attributable to Infection with This Organism, J. Prev. Med. **3**:159 (March) 1929.

4. Morgan, H. de R., and Ledingham, J. C. G.: The Bacteriology of Summer Diarrhea, Proc. Roy. Soc. Med. (Epidemiol. Sect.) **2**:133 (Feb. 26) 1909.

ered from the controls. Three-tenths cubic centimeter of a twenty-four hour broth culture of four of the five strains isolated from the sick children killed mice weighing between 10 and 15 Gm. in sixteen to twenty-four hours. The organism was recovered in pure culture from the heart's blood. The fifth mouse was made sick with this amount of broth culture but recovered in forty-eight hours. Five-tenths cubic centimeter, however, promptly killed a mouse; the organism here too was recovered in pure culture from the heart's blood.

Of the ten strains recovered from the controls, seven were pathogenic for mice when 0.3 cc. of a twenty-four hour broth culture was injected intraperitoneally. Five-tenths cubic centimeter was necessary to kill two of the others, and one strain failed to kill when 1 cc. was injected. In all the mice that died the organism was recovered from the heart's blood in pure culture.

I conclude that the pathogenicity of the organism for mice by intraperitoneal injection is of no value in determining the pathogenicity for man.

IS BACILLUS MORGANI I PATHOGENIC FOR MAN?

The proof that B. Morgani I is a pathogen, adduced by Morgan and Ledingham [4] from their studies of the bacteriology of summer diarrhea, rested mainly on the comparative frequency of isolation of the organism from the stools of sick children and of controls. In 1905 they recovered it once from twenty normal infants. In 1908 they recovered it twelve times from ninety-nine children and once from thirty-three children during the spring. From the stools of sick children they isolated the organism in 54 per cent in 1905, 56 per cent in 1906, 16 per cent in 1907 and 53 per cent in 1908.

Alexander [5] reported that in 1911-1912 B. Morgani I was found in the stools of 4 per cent of normal children and in the stools of 13.4 per cent of children suffering from diarrhea.

Lewis [6] in 1910 failed to isolate the organism from the stools of normal children but found it in those of 30 per cent of children suffer-

5. Alexander, D. M.: Report on the Prevalence and Character of Non-Lactose-Fermenting and Non-Liquefying Aerobic Bacilli in the Faeces of Young Children Under Normal Conditions and in Epidemic Diarrhoea During 1911, Forty-First Ann. Rep. M. Off. Local Gov. Bd., London, 1911-1912, append. B, no. 3, p. 288. Report on the Prevalence and Character of Bacilli Occurring in the Faeces of Young Children Under Normal Conditions and in Epidemic Diarrhoea, Forty-Second Ann. Rep. M. Off. Local Gov. Bd., London, 1912-1913, append. B, no. 4, p. 384.

6. Lewis, C. J.: Report on the Results of an Examination of the Faeces of Children with Special Reference to the Occurrence of Bacilli Which Neither Liquefy Gelatin Nor Ferment Lactose, Fortieth Ann. Rep. M. Off. Local Gov. Bd., London, 1910-1911 (supp.), append. B, no. 2, p. 314.

ing from diarrhea. In 1911 he found it in 17 per cent of normal children and in 70 per cent of those with diarrhea. Nabarro [7] did not isolate B. Morgani I in one hundred and seven cases of summer diarrhea in 1921. Lewis [8] in 1911 found it in 95 per cent of cases of infantile diarrhea and in only 38 per cent of the children of the same population. He also found it in seventeen of twenty-eight samples of milk in Birmingham.

In my series of cases from the Home for Hebrew Infants I recovered the organism from the stools of five of six patients with infantile diarrhea. From twenty-one subjects who were normal, lived in the same environment and ate food prepared in the same diet kitchen, I recovered B. Morgani I fifteen times.

In 1906-1907 Morgan,[9] investigating the bacteriology of summer diarrhea in infants, isolated an organism from the stools of 54 per cent of the sick infants which he believed responsible for the disease. The organism had not been previously described. It was a gram-negative organism, slightly motile; it fermented dextrose with the production of acid and a small amount of gas and levulose and galactose with the production of acid and gas. On litmus milk it produced alkalinity in three days.

Castellani and Douglas [10] amplified the description to include the production of very slight amounts of gas on one pentose, arabinose. They stated that acid but not gas may be formed by the organism from glycerin and that acid may be formed from xylose and amygdalin in from seven to twenty-one days.

Bergey [1] classified the organism as a member of the Salmonella group. Ohrum and Bahr,[11] Bahr and Thomsen,[12] Thjötta [13] and D'Aunoy [14]

7. Nabarro, D.: Summer Diarrhoea, Brit. M. J. **2**:857 (Nov. 10) 1923.

8. Lewis, C. J.: Report on the Prevalence and Character of Non-Lactose Fermenting and Non-Liquefying Aerobic Bacilli in the Faeces of Young Children Under Normal Conditions and in Epidemic Diarrhoea During 1911, Forty-First Ann. Rep. Local Gov. Bd., London, 1911-1912, append. B, no. 2.

9. Morgan, H. de R.: The Bacteriology of the Summer Diarrhea of Infants, Brit. M. J. **1**:908, 1906; The Bacteriology of the Summer Diarrhea of Infants, ibid. **2**:16 (July 6) 1907.

10. Castellani, A., and Douglas, M.: Serological Studies on Bacillus Morgan No. 1 (Salmonella Morgagni Cast. and Chalm.), J. Trop. Med. **35**:161 (June) 1932.

11. Ohrum, T., and Bahr, O. F.: Meddelelse fra det Kgl. Veterin. og Landbohojskoles Serum Laboratorium, no. 5, 1910, p. 210.

12. Bahr, O. F., and Thomsen, T.: Meddelelse fra det Kgl. Veterin. og Landbohojskoles Serum Laboratorium, no. 19, 1912, p. 66.

13. Thjötta, T.: Bacillus of Morgan No. 1: Meta-Colon-Bacillus, J. Bact. **5**:67 (Jan.) 1920.

14. D'Aunoy, R.: Infections Probably Due to Morgan's Bacillus, Am. J. M. Sc. **178**:834 (Dec.) 1929.

expressed the belief that the organism should be classed in the metacolon group despite the fact that it does not ferment lactose. They believed that the better classification would be Escherichia Morgagni.

Thjötta [13] stated that while there is a definite serologic association of the strains of all the intestinal pathogens it is impossible to find such an association in the strains of B. Morgani I. Agglutinins for any single organism agglutinate the homologous strain only and show little or no power to agglutinate heterologous strains of B. Morgani I. He regarded this point as one of great importance since such behavior in agglutinins is characteristic of Bacillus coli. All the other members of the Salmonella group agglutinate readily and in high dilutions of heterologous immune serums.

Castellani and Douglas [10] concluded that the term B. Morgani I includes at least five separate antigenic strains, probably more. They stated that the absorption test shows that there are slight but rather complex relationships among them. In none of the other reports was mention made of more than one sample of stool from the same child having been examined. Morgan and Ledingham [4] kept their samples in the icebox and replated from the one sample if nonlactose fermenters were not found. These investigators mentioned the work of Booker in America who in 1887 made the first attempt on a large scale to investigate the bacteriology of summer diarrhea. They mentioned and confirmed his observation that the normal flora of the intestinal tract diminishes in number in diarrheal feces, its place being taken by organisms that occur inconstantly in the healthy intestine. Thus B. coli and Bacillus lactis-aerogenes which occur in large numbers in the normal stool are seen much less frequently in diarrheal stools, their place being taken by nonpathogenic members of the Escherichia and Aerobacter groups that are normal inhabitants of the intestinal canal.

It is probable that B. Morgani I is a normal inhabitant of the intestinal canal. It is also probable that careful and repeated search will reveal its presence in every normal infant. The relative ease with which it can be recovered from diarrheal feces is dependent on the decrease in the normal flora in such stools plus the peculiar ability of B. Morgani I to thrive in the inflamed intestine. Thjötta,[13] summarizing the proofs of the pathogenicity of B. Morgani I, concluded that there is nothing to prove that the metacolon organism is more than a saprophytic colon bacillus that thrives especially well in the inflamed intestine.

Demonstration of the pathogenicity of an organism for man must rest on firmer proof than the relative frequency of its recovery from the stools of sick persons. If the organism is recovered from the blood stream, if there is serologic evidence such as agglutination of the homologous organism by the serum of the patient in high dilution, if it is recovered from morbid processes taking place inside the body, as from

an abscess or from the spinal fluid, the proof of pathogenicity is on a firmer basis. The final proof, of course, depends on the infection of man with the organism and its recovery from the diseased person.

Kligler [15] stated: "It is evident that the etiological significance of Morgan's bacillus is by no means established. Neither Morgan nor Lewis was able to demonstrate the specific antibodies in the sera of children from whom the bacilli were isolated." Kligler found a wide diversity of the antigenic properties of the organism. He stated that this raises the question of specific relationship to a pathologic process in man.

Thjötta [16] in 1918 studied nine patients with severe colitis and recovered B. Morgani I from all. No agglutinins for the organism were found in the blood of any of the patients. He concluded that in the absence of specific antibodies it is reasonable to believe that B. Morgani I was not the cause of the disease but was a saprophyte that grew particularly well in the inflamed intestine. Thjötta [16] in 1928 reported a case of sepsis in which B. Morgani I was recovered from the gallbladder and from the blood. The blood agglutinated the organism at 1 : 320.

Fridtjof Bang [17] denied that a relationship existed between Morgan's bacillus and infantile diarrhea. He seriously considered the bacillus as a rare type of B. coli.

Gittins and Hawksley [18] reported on a case of meningitis and septicemia due to B. Morgani I. Their paper did not include a report of the agglutinating power of the blood against the organism recovered. Dick, Dick and Williams [19] reported an epidemic of enteritis associated with mastoiditis that they believed was due to B. Morgani I. Their grounds for this belief are doubtful, as they are based merely on the recovery of the organism from the intestines in five fatal cases. The recovery was made from the intestinal contents after death. No studies were made during life, and none of the other children in the ward were examined as controls.

D'Aunoy reported three cases of infection probably due to Morgan's bacillus. In one case the organism was isolated from the blood, in one from the urine and in one from the stool. Agglutination was present in all three cases, in a dilution ranging from 1 : 120 to 1 : 240.

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15. Kligler, I. J.: Agglutination Reactions of Morgan Bacillus No. 1, J. Exper. Med. **29**:531 (June) 1919.

16. Thjötta, T.: Septic Infection Due to Bacterium morgani 1, J. Infect. Dis. **43**:349 (Oct.) 1928.

17. Bang, F.: Meddelelse fra Statens Seruminst. Copenhagen **9**:157, 1917.

18. Gittins, R., and Hawksley, J. C.: Meningitis and Septicemia Due to Morgan's No. 1 Bacillus, Lancet **1**:1040 (May 14) 1932.

19. Dick, G. G.; Dick, G. H., and Williams, J. L.: The Etiology of an Epidemic of Enteritis Associated with Mastoiditis in Infants, Am. J. Dis. Child. **35**:955 (June) 1928.

Havens and Ridgway [3] reported a group of thirteen cases. In five of the thirteen blood cultures were positive, and in nine cases in which the serum was tested agglutination of the organism took place in dilutions of from 1:40 to 1:160.

Sutton [20] reported the case of a patient with pseudomembranous enterocolitis and mastoiditis associated with infection with Morgan's bacillus. This is a doubtful case. The stools were examined once during life, and B. Morgani I was not found. The organism was recovered from the middle ear shortly before death and from the heart's blood at autopsy five and one-half hours after death. The pus from the ear and the blood from the heart showed also a nonhemolytic streptococcus. The organism was not looked for in the pseudomembrane in the jejunum and colon, no agglutination studies were done and the finding of more than one organism in the heart's blood weakens the proof. The presence of B. Morgani I in the ear may have been the result of a preagonal invasion, or the organism may have been from regurgitated intestinal contents that found access to the middle ear through the eustachian tube.

The weight of evidence is that B. Morgani I is a normal inhabitant of the intestinal canal, that it is found more frequently during periods of diarrhea due to a suppression during such periods of the normal intestinal flora, that it may occasionally assume pathogenic properties and that evidence of its having become pathogenic cannot be based on its mere recovery from the stool. Evidence to be conclusive must include recovery of the organism from the infected person and its specific agglutination by the serum of the patient.

In the epidemic studied by me, had the results of the cultures from the stools of the sick infants not been controlled by examination of the well children in the ward, whose food came from the same diet kitchen and whose general care was identical with that of the sick infants, considerable support would have been given to the statement of Johnston, Brown, Tisdall and Fraser [21] that "acute intestinal intoxication, fermentative diarrhea, infectious diarrhea, and summer diarrhea are synonyms indicating one condition—a gastro-intestinal infection with species of the colon-paratyphoid-dysentery group of bacilli." They expressed the belief that there is no causal connection between the infection of the upper respiratory tract and the diarrhea. They examined the stools of one hundred and seventy-two patients with acute intestinal intoxication or related conditions. One hundred and seven controls were also studied. Micro-organisms of definitely recognized pathogenicity were isolated in

20. Sutton, T. L.: Pseudomembranous Enterocolitis and Mastoiditis Associated with Infection with Morgan's Bacillus, Am. J. Dis. Child. **37**:814 (April) 1929.

21. Johnston, M. M.; Brown, A.; Tisdall, F. F., and Fraser, D. T.: Intestinal Infections in Infants, Am. J. Dis. Child. **45**:1 (Jan.) 1933.

twenty-seven of the patients. Species of "probable" significance, excluding B. Morgani I and B. paracoli, were isolated in forty-three cases; in forty-two cases no suggestive micro-organism was revealed.

The organisms of well recognized pathogenicity were Bacillus dysenteriae (Sonne, Hiss-Russel, and Flexner), Bacillus paratyphosus B and Bacillus paratyphosus C. Those of doubtful pathogenicity were: Bacillus Schmitzii, Bacillus dispar, P. asiaticus, B. Morgani, B. paracoli, Fothergill's bacillus and the proteolytic bacilli.

No criticism can be made of the diagnosis in the twenty-seven cases in which proved pathogens were isolated. However, since no serum was found to contain agglutinins for Bacillus dysenteriae Schmitz, P. asiaticus, B. dispar, B. paratyphosus C or the proteolytic bacteria, their pathogenicity in these cases must indeed be considered doubtful. Fothergill's bacillus was isolated from eleven of the sick children. In seven cases the agglutination reaction was tested and in two the results were positive in a dilution of 1:160. Fothergill's bacillus was not isolated from the controls, but the serum of three of twelve persons tested showed a positive agglutinin reaction, twice in a 1:20 and once in a 1:160 dilution.

B. Morgani I was isolated from fifty-seven patients and fourteen controls. Of forty cases in which the culture of the stool was positive agglutination by the homologous serum was present in only two, once in a 1:80 and once in a 1:160 dilution.

One can see, therefore, that definite pathogens were found in only twenty-seven of one hundred and seventy-two cases. The possible pathogenicity of the remaining micro-organisms does not rest on a firm basis in the absence of the demonstration of agglutinins in the serum of the patients. This doubt is further increased by the demonstration of agglutinins for Fothergill's bacillus in the serum of three of the controls.

Largely as the result of the work done by Johnston, Brown, Tisdall and Fraser, the theory sponsored by Marriott [22] that there is a causal connection between otitis media or mastoiditis and acute gastro-enteritis has given way to the belief that the two conditions are independent and that the gastro-enteritis results solely from enteral infection by members of the dysentery-paratyphoid-colon group of organisms.

That there is a clinical association between the two conditions can hardly be doubted. Mitchell and his co-workers [23] have pointed out that

22. Marriott, W. M.: Observation Concerning the Nature of Nutritional Disturbances, Laryngoscope **35**:592 (Aug.) 1925.

23. Mitchell, A. G.; McCarthy, M. F.; Leichliter, J. W., and Seinsheimer, F.: Otitis Media and Its Relation to Gastro-Enteritis, J. A. M. A. **92**:970 (March 23) 1929.

there are but four possible explanations for the observed coexistence of these diseases: 1. The infection in the middle ear may cause the gastro-enteritis. 2. The gastro-enteritis may cause the condition in the middle ear. 3. The same cause may explain both. 4. They may be independent diseases. These workers expressed the belief that no one cause can explain every case.

With the conclusion of Mitchell and his co-workers I am in complete agreement. Some cases undoubtedly can be explained on the basis of a gastro-intestinal infection by a known pathogenic organism. The resulting dehydration and acidosis may in those cases lower the resistance sufficiently that otitis media may occur secondarily. The fact that there is no similarity of bacterial flora in the ear and in the intestinal tract does not rule out the possibility that an infection of the upper respiratory tract or otitis may cause diarrhea. There is a possibility that the absorption of toxins from an inflammation in the upper respiratory tract may initiate diarrhea. There is also the possibility that the diarrhea in such cases may be an expression of an allergy and that the diarrhea is of allergic origin. To support this might be brought the common observation that in children under 2 years of age the first sign of a cold or infection of the upper respiratory tract is commonly a foul-smelling, loose stool with much mucus. This is often the first indication of the disease in young infants and may precede visible redness of the throat by only a few hours.

At the beginning of each winter there is a house epidemic of colds accompanied by diarrheal, evil-smelling, mucous stools. The almost simultaneous appearance of the infection of the upper respiratory tract and the abnormal stools clearly shows the extreme sensitivity of the gastro-intestinal tract to infection of the upper respiratory tract. Whether this is due to the direct action of the cold virus or whether it is an allergic manifestation is difficult to decide, but the fact that one or more stools of the type described accompany a cold in the great majority of infants under 2 years of age is undoubted.

The epidemic reported in this paper was, in my opinion, an epidemic of infection of the upper respiratory tract. B. Morgani I bore no etiologic relationship to the diarrhea. The diarrhea must be accounted as a secondary manifestation of infection in the upper respiratory tract.

SUMMARY

1. B. Morgani I was isolated from the stools of five of six infants with gastro-enteritis associated with infection of the upper respiratory tract.

2. B. Morgani I was isolated from the stools of fifteen of twenty-one controls.

3. B. Morgani I was isolated from the stools of fourteen of thirty-eight infants from a well baby clinic.

4. B. Morgani I, B. paracoli and P. asiaticus can be recovered with much greater frequency than previously reported if repeated cultures of the stools are made.

5. B. Morgani I, like B. coli not normally pathogenic for man, may assume pathogenic characteristics in a small number of cases.

6. The mere recovery of B. Morgani I from the diarrheal stool is not proof of its pathogenicity. This is also true for the following organisms: B. paracoli, P, asiaticus, B. dysenteriae Schmitz, B. dispar, B. paratyphoid C and the proteolytic bacteria.

7. Additional evidence must be obtained to prove the pathogenicity of these organisms, namely, agglutination in high dilution with the blood serum of the suspected patient.

8. The close clinical relationship of otitis media and infection of the upper respiratory tract to diarrhea in infants under 2 years of age is probably not due to infection of the intestinal tract with pathogenic organisms in the great majority of cases.

9. The clinical relationship may be the manifestation of allergy or of absorption of toxins from a pathologic process in the upper respiratory tract.

LATENT CARDIAC COMPLICATIONS FOLLOWING SYDENHAM'S CHOREA

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In considering the etiology of Sydenham's chorea, the majority of observers are of the opinion that all such chorea is of rheumatic origin. This opinion is based largely on the fact that there is frequent involvement of the heart. Yet in all other respects, chorea differs from the clinical picture of rheumatism as seen in childhood. One is inclined to wonder, therefore, whether some of the cases of ordinary chorea in childhood are caused by another virus than that of rheumatism. In reviewing the histories of a large number of cases of chorea one sees numerous instances in which chorea is the only manifestation of disease, unattended by arthritic symptoms or other evidences of rheumatic infection. In apparent contrast to these instances are the many cases of chorea which either follow or precede a typical attack of rheumatic fever with cardiac involvement, or in which successive attacks of rheumatic fever and of chorea alternate with one another or occur together; one often sees both of the conditions actually occurring together during the primary illness, as indicated by the appearance of fever, pains in the joints or muscles, purposeless movements and evidences of endocarditis or pericarditis.

It is not always possible to establish a diagnosis of rheumatic fever in suspected cases. Fever, pains in the muscles and joints, rapid pulse, lesions of the skin and even electrocardiographic evidence cannot be relied on for definite diagnosis unless there occur also an organic lesion of the heart or typical subcutaneous nodules. In fact, organic cardiac changes may be considered to outrank the subcutaneous nodules in diagnostic importance, since in this climate the nodules do not occur unless a cardiac lesion is present as well. To the pathologist also the presence of a typical lesion of the heart valves or of the heart muscle remains the only satisfactory proof of the previous existence of rheumatic infection.

As the knowledge of rheumatic fever has grown, the heart has come to occupy the center of interest in the study of this disease. Not only is it a means of diagnosis par excellence, but it is a sensitive recorder of

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the progress of the disease to the final stages. It is a common experience at autopsy to see in the valves evidences of repeated attacks, in spite of the fact that there were few or no clinical evidences of recurrent infection during life. Often an acute verrucous endocardial lesion is found in persons dying of wholly unrelated conditions. To such observations is due the concept of chronicity in rheumatic infection, and with justice one may say in most instances, "once rheumatic, always rheumatic." If the early involvement of the valves of the heart is mild, it is apparent that it may take years before successive attacks produce sufficient valvular deformity to be recognizable clinically. For these reasons it is never possible to say definitely that a patient with rheumatism is cured.

In the light of such knowledge one is better prepared to study the relation of Sydenham's chorea and rheumatic fever. If chorea is a separate disease one may expect the end of the choreiform movements to signify the end of the disease. If, on the other hand, chorea is part of rheumatism, one may expect proof of this in the form of an organic cardiac lesion.

Eighty-four cases of chorea were available to us for study. Of these 9 cases fell into the group in which manifest rheumatism was also present, either before or subsequent to the appearance of chorea, with a high expectation of cardiac disease (Pfaundler[1]). Seventy-five cases remained which we selected for particular study because they presented only the single symptom of choreiform movements over a period of years. Subsequent studies of the cases of "pure" chorea were made chiefly in order to learn in how many of the cases organic lesions of the heart eventually developed. We realize that the term "pure" is open to objection because of the possibility that in many of the cases attacks of rheumatic fever may have occurred under the mask of infections of the upper respiratory tract or of grip; however, the term is useful in order to emphasize the distinction we wish to make between chorea occurring without evident rheumatic symptoms, as in the cases of "pure" chorea, and chorea occurring in the course of an obvious rheumatic syndrome.

In the cases of the present study, the diagnosis of an organic cardiac lesion was based on a number of criteria. It is often difficult to determine by simple examination whether or not an organic lesion is present. During the earlier weeks of the first attack of chorea such a diagnosis must be based on purely clinical reasoning, in relation to which the history is of great importance. Murmurs at the base are so common in normal children that they may be disregarded; likewise, accentuation of the second pulmonic sound may be disregarded.

1. Pfaundler, M.: Akuter Gelenkrheumatismus und Chorea minor, Ztschr. f. Kinderh. **30**:274, 1921.

A systolic murmur at the apex, however, must be taken seriously in a case of chorea. Enlargement of the heart is difficult to prove unless it is marked. During the first attack of chorea, therefore, we have been content to regard as of special significance all systolic murmurs heard within the mitral area, whether transmitted to the left or not and irrespective of the presence in the same region of an accompanying split

TABLE 1.—*Distribution of Seventy-Five Cases of Sydenham's Chorea According to the Period of Observation*

Period of Observation, Years	Number of Cases
1	6
2	7
3	14
4	9
5	10
6	8
7	5
8	13
9	2
12	1
Total	75

TABLE 2.—*Observations of Cardiac Complications Following Sydenham's Chorea*

Number of Patients Observed	Period Observed, Years	Number of Patients with Murmurs at First Attack	Number of Patients with Murmurs Subsequently Developing	Total Number of Patients with Cardiac Murmurs	Number of Patients with Additional Attacks of Chorea	Number of Patients with Electrocardiographic Evidence of Cardiac Disease	Number of Patients with Roentgenographic Evidence of Cardiac Disease
6	1	1	2	3	0	0	3
7	2	0	4	4	2	0	4
14	3	8	2	10	0	5	8
9	4	5	3	8	0	1	4
10	5	4	2	6	4	2	2
8	6	4	2	6	2	1	4
5	7	5	0	5	0	2	2
13	8	8	5	13	3	2	10
1	10	1	0	1	0	1	0
1	11	1	0	1	0	1	1
1	12	1	0	1	0	0	1

second sound. Our experience agrees with that of St. Lawrence in the observation that many of the murmurs which are heard during the first attack of chorea disappear after the attack has subsided, only to reappear later at subsequent examinations. This observation coincides also with our experience in cases of rheumatic fever, in which we have often been surprised at the disappearance of well marked evidences of cardiac involvement a year or so after the attack of rheumatism.

In cases of chorea which are observed from year to year, the criteria for the diagnosis of organic lesions of the heart are much more num-

erous. An arrhythmia may be noted from time to time. An early sign which should arouse suspicion is an impure sound at the apex; this is often audible many months before a definite systolic murmur is detected. The systolic murmur may or may not be transmitted to the left. Later, a split second sound may be heard at the apex as the forerunner of a presystolic murmur.

In the cases of "pure" chorea in the present study, observations of interest because of their lack of pathologic significance were noted. In no cases were aortic murmurs detected; neither were signs of pericarditis obtained or subcutaneous nodules noted in spite of careful search. We

TABLE 3.—*Incidence of Cardiac Involvement in Chorea*

Type of Cardiac Involvement	Number of Cases
Systolic murmur present after from one to fifteen years	58 (77.3%)
Murmurs present at the first attack	38
Murmurs subsequently developed	20
Systolic murmurs and roentgenographic evidence of cardiac disease	39
Total number	75

TABLE 4.—*Composite Follow-Up Data on Cardiac Involvement in Chorea*

Number of Cases of Chorea in Each Group	Period of Observation, Years	Cases with Murmurs	
		Number	Per Cent
6	1	3	50
7	2	4	57
14	3	10	72
9	4	8	89
10	5	6	60
8	6	6	75
5	7	5	100
13	8	13	100
5	9-12	3	100
Total 75	2-12	58	77.3

have no explanation for these facts, although it is possible that they indicate a milder form of rheumatism. Roentgen examination of the heart proved of assistance to us in many of the cases, and in a surprising number the roentgenograms showed definite abnormalities in the size and the contour of the heart, as indicated in the tables. In all of the cases with positive roentgenographic findings the pulmonary conus was prominent. The roentgenographic appearance of the heart in these cases was particularly interesting because of the striking similarity of the roentgenograms to one another, each plate seeming to be the replica of the next. Electrocardiographic evidence of cardiac disease was obtained in certain cases; little help was obtained from this source, however, except in cases in which the patient was frequently tested.

COMMENT

It is surprising how few reports are to be found in the literature dealing with follow-up studies of cases of so-called "pure" chorea. The same thing may be said for chorea in general; although many studies have been made in connection with the incidence of heart disease in chorea, in few of these cases has the cardiac condition been under observation for a considerable length of time. In 1887, Stephen MacKenzie [2] reported 31 cases of chorea which he had observed for five years; in 60.6 per cent of these there were cardiac lesions. Donkin [3] examined 42 children who had suffered from chorea from two to twelve years previous to examination, and he found that 18, or 42 per cent, of them suffered from cardiac involvement. Osler's [4] excellent study of chorea included 140 cases; the patients were examined from two to sixteen years after the initial attack of chorea. The heart was reported as normal in 51 of these cases, or in 36.4 per cent. Organic lesions of the heart were noted in 72 cases, or in 51 per cent, and functional cardiac disturbance was observed in 17 cases. If it is taken into account that Osler preferred to err on the side of conservatism in excluding the 17 cases, though he expressed doubt of the nature of the cardiac disturbance in many of them, it is possible that with the newer knowledge of rheumatism these cases, too, might have been included in the group of those with organic cardiac disease, thus raising the ratio of cardiac involvement to 63 per cent. Thayer,[5] in 1906, published a report of a large group of cases, but the subsequent period of observation was too short for comparison. Abt and Levenson,[6] in 1916, analyzed 226 cases of chorea, in 73 of which, or in 37 per cent, evidences of cardiac involvement were present at the time of the first examination. Wilson, Lling and Croxford,[7] studied the problem from a slightly different standpoint; 177 patients with known cardiac disease were examined for

2. MacKenzie, Stephen: Report on Inquiry: II. Chorea, Brit. M. J. **1**:425 (Feb. 19) 1887.

3. Donkin, H. Bryan: Diseases of Childhood, New York, William Wood & Company, 1893, p. 302.

4. Osler, William: Cardiac Relations of Chorea, Am. J. M. Sc. **94**:371 (Oct.) 1887; On Chorea and Choreiform Affections, Philadelphia, P. Blakiston's Son & Co., 1898.

5. Thayer, W. S.: An Analysis of Eight Hundred and Eight Cases of Chorea with Special Reference to the Cardio-Vascular Manifestations, J. A. M. A. **47**: 1352 (Oct. 27) 1906.

6. Abt, Isaac A., and Levenson, A.: A Study of Two Hundred and Twenty-Six Cases of Chorea, J. A. M. A. **67**:1342 (Nov. 4) 1916.

7. Wilson, May G.; Lling, Claire, and Croxford, Geneva: Heart Disease in Children, Am. Heart J. **4**:164, 1928.

manifestations of chorea, which were found to be present in 42 per cent; chorea was the only finding in addition to the cardiac condition in 14 per cent.

It is evident from the data on our own group of 75 cases of "pure" chorea that cardiac lesions occur with great frequency, as judged by clinical evidence. In many instances cardiac involvement developed insidiously, without recognizable attacks of rheumatic fever and in some cases without further attacks of chorea. This type of cardiac involvement, as is well known, progresses slowly and without great restriction in cardiac function. The number of cases in each yearly group is too small for definite conclusions, but it will be of interest to follow a group such as ours for a period of twenty years or more, in order to see in how many cases the process continues and in how many the murmurs disappear.

CONCLUSIONS

Seventy-five cases of so-called "pure" chorea were observed for from one to twelve years for evidence of cardiac involvement.

The term "pure" chorea was used for the cases of chorea in which no other manifestations of rheumatism were noted clinically.

Cardiac involvement was diagnosed by physical signs, roentgen examination and electrocardiography.

The most constant physical sign was a systolic murmur of marked persistence at the apex; at times it was transmitted to the left, but often it was not.

Electrocardiographic findings were helpful in the diagnosis of some of the cases; this part of the study has not yet been completed.

Roentgenographic evidence of cardiac lesions was remarkably constant and corresponded well with the physical findings; occasionally, positive roentgenographic evidence was found in cases with physical findings of no significance.

The longer the period of observation after the first attack of chorea, the higher was the percentage of cardiac involvement found; it apparently approached 100 per cent after seven or eight years, although the number of cases studied is too small to permit a definite statement.

The signs of cardiac involvement developed insidiously, without recognizable attacks of rheumatic fever and in some cases without further attacks of chorea.

In this series aortic murmurs, pericarditis and subcutaneous nodules were never encountered.

It seems probable that what is said of rheumatic fever may also be said of chorea: "The heart is always involved." This probable cardiac involvement is added evidence that Sydenham's chorea is of rheumatic origin.

MINERAL METABOLISM IN OSTEOGENESIS IMPERFECTA

A SUMMARY WITH REPORT OF A CASE

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AND
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The knowledge of mineral metabolism in osteogenesis imperfecta has been obtained mainly from the investigations of Schwarz and Bass,[1] Bookman,[2] and Klercker [3] and recently from a more detailed study by Sindler.[4] A summary and comparison of their data with a study of the metabolism in a similar case are presented in this paper. Only by thus summarizing the data and by adding more complete analyses will an approach to the study of this baffling disease yield its store of information. No attempt has been made to review the clinical and pathologic literature on the subject since this has been done recently by Dietrich.[5]

We were fortunate in being able to study soon after birth a female infant who showed all the clinical signs of osteogenesis imperfecta. The clinical diagnosis was further verified by the roentgenogram, as shown in the figure.

REPORT OF A CASE

The infant was given powdered milk on the tenth day of life, and metabolism experiments were started on the fourteenth day. Experiments were carried out during three control periods, one of four days and two of six days each. The infant was then given 10 drops of viosterol three times a day, and metabolism studies were carried out for three more six day periods. An analysis was made of the food, urine and stools to determine the nitrogen, calcium, phosphorus, magnesium, sodium, chlorine, potassium and sulphur content. The difference

1. Schwarz, H., and Bass, M.: Osteogenesis Imperfecta: Report of a Case with the Study of Its Metabolism, Am. J. Dis. Child. **5**:131 (Feb.) 1913.

2. Bookman, A.: The Metabolism in Osteogenesis Imperfecta with Special Reference to Calcium, Am. J. Dis. Child. **7**:436 (June) 1914.

3. af Klercker, K. O.: Zur Kenntnis des Stoffwechsels, besonders des Mineralstoffwechsels bei Osteogenesis imperfecta, Monatschr. f. Kinderh. **25**:338, 1923.

4. Sindler, A.: Der Stoffwechsel bei Osteogenesis imperfecta, Ztschr. f. Kinderh. **42**:85, 1926.

5. Dietrich, A.: Die Entwicklungsstörungen der Knochen, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1929, vol. 9, p. 198.

between the amount of these substances in the food and that found in the excretions was taken to be the amount retained. The analytic methods used for the various determinations were described in a previous paper.[6]

The infant at birth weighed 2,750 Gm. and when 3 months old, 3,320 Gm. At this time the experimental study ended because of fever. The infant lived for a week longer and died of otitis media on the left side and bronchopneumonia.

The blood calcium content at the beginning of the study was 8.4 mg. per hundred cubic centimeters, and the phosphorus content, 6.7 mg.

Roentgenogram of a child with osteogenesis imperfecta.

COMMENT

In table 1 are to be found the mineral values obtained from the literature for infants with osteogenesis imperfecta together with the data from our study. It is difficult to compare the various data since the infants were not all on the same feeding nor were they of the same age. Wyatt

6. Iob, Vivian, and Swanson, W. W.: Mineral Growth of the Human Fetus, Am. J. Dis. Child. **47**:302 (Feb.) 1934.

TABLE 1.—*Daily Retention of Minerals by Normal Infants and Infants with Osteogenesis Imperfecta*

Condition of Infant	Age	Type of Feeding	Calcium*	Magnesium	Phosphorus	Sulphur	Sodium	Potassium	Chlorine	Nitrogen	Author	No. of Period	Length of Periods, Days	Comment
Normal.....	1 to 3 mo.	Breast milk	0.10	0.20	0.81	0.27	2.53	2.50	2.02	40.4	Swanson	..	6	Average of several 6 day periods
Normal.....	1 to 3 mo.	Breast milk	2.03	0.29	2.38	0.65	2.50	3.29	2.85	43.2	Swanson and Iob	..	6	Average of several 6 day periods
Osteogenesis imperfecta	3 wk.	Breast milk	0.70	1.04	1.41	....	—0.36	1.40	3.90	23.3	Sindler	1	5	No calcium given
Osteogenesis imperfecta	4 wk.	Breast milk	3.30	0.89	1.11	....	—0.87	1.15	3.10	1.98	Sindler	2	5	1 Gm. calcium citrate daily
Osteogenesis imperfecta	5 wk.	Breast milk	1.09	1.07	1.25	....	0.28	1.21	5.10	22.3	Sindler	3	4	
Osteogenesis imperfecta	4 mo.	Breast milk	1.98	1.14	3.04	....	....	....	....	39.5	Klercker	1	6	Average of two 3 day periods
Osteogenesis imperfecta	4 mo.	Breast milk	1.32	0.64	2.13	....	—0.90	1.19	....	20.6	Klercker	2	6	Average of two 3 day periods
Osteogenesis imperfecta	5 mo.	Breast milk	2.35	0.92	2.90	....	1.51	1.72	—0.20	20.6	Klercker	..	4	Average of six 4 day periods
Osteogenesis imperfecta	7 mo.	Breast milk	1.61	0.39	0.88	0.66	3.70	1.30	....	30.3	Schwartz and Bass	..	6	
Normal.....	1 to 3 mo.	Cow's milk	2.87	0.82	2.97	0.65	4.87	4.56	4.84	66.6	Swanson	..	6	
Osteogenesis imperfecta	10 wk.	Cow's milk	0.96	0.23	3.44	0.66	....	....	....	34.1	Bookman	1	6	
Osteogenesis imperfecta	.....	Cow's milk	7.17	0.81	6.86	2.96	....	....	....	57.3	Bookman	2	6	1.7 Gm. calcium lactate daily
Osteogenesis imperfecta	3 wk.	Cow's milk	0.79	0.10	1.15	—0.15	0.25	1.97	0.60	80.4	Swanson and Iob	1	4	
Osteogenesis imperfecta	4 wk.	Cow's milk	2.00	0.28	2.61	0.38	2.03	3.85	3.48	81.7	Swanson and Iob	2	6	
Osteogenesis imperfecta	5 wk.	Cow's milk	1.80	0.18	1.35	0.12	1.14	1.80	1.59	62.9	Swanson and Iob	3	6	
Osteogenesis imperfecta	3 mo.	Cow's milk	2.15	0.28	2.50	0.13	2.47	3.98	2.45	85.8	Swanson and Iob	4	6	30 drops viosterol daily
Osteogenesis imperfecta	3 mo.	Cow's milk	2.12	0.28	2.14	0.62	1.53	3.22	2.06	90.1	Swanson and Iob	5	6	30 drops viosterol daily
Osteogenesis imperfecta	3 mo.	Cow's milk	2.05	0.18	2.05	0.01	—0.29	2.73	1.17	80.3	Swanson and Iob	6	6	30 drops viosterol daily

* The values for all the minerals are expressed in millimols.

and McEachern [7] have contended that the studies of the mineral content made so far have given inconclusive results. A glance at table 1, showing most of the available data, apparently confirms their contention. There are, however, certain interesting deviations from the norm which we wish to point out. Apparently the retention of calcium and phosphorus in osteogenesis imperfecta is somewhat low. No conclusions can be drawn, however, since our findings and those of other investigators have shown marked variations when normal infants were fed breast milk or cow's milk. The fluctuation in the values for magnesium may be attributed partly to the difficulty encountered in determining this substance. Most of the values for sulphur, we think, are well within the normal range. The figures for retention of sodium reveal the greatest fluctuation shown by any mineral determined. The retention was frequently low, and in several instances there was a negative balance. In our patient the low or negative balance of sodium may have been due to the poor gain in weight, but this cannot be true of the patient in Sindler's case in whom an excellent gain in weight occurred. The retention of potassium and chlorine appears to have approached the normal values except for the finding of retention of chlorine in the case of the 7 month old infant reported on by Klercker. The retention of nitrogen was apparently normal except by the infant in our case in whom for some unexplained reason it was considerably above the normal value.

In table 2 we have summarized the results of the known analyses of normal bone and compared them with the values for bone from patients with osteogenesis imperfecta. The total ash content of bone from patients with osteogenesis imperfecta is about 30 per cent below that of normal bone. In this respect only does our analysis compare with that of Sindler. In analyzing for the various mineral components we were unable to confirm the high sodium and potassium content reported by Sindler. Furthermore, our analyses of bone did not reveal the marked decrease in calcium or the increase in magnesium which he found.

In table 3 we have compared the percentage composition of normal bone with that of bone of patients with osteogenesis imperfecta. It will be seen that the proportional relationship between calcium and phosphorus was disturbed in two out of three cases in that the phosphorus content was in excess of the normal value and the calcium content was materially reduced. In the case of osteogenesis imperfecta reported by Wyatt and McEachern the percentages compare well with those obtained for normal bone. In tables 2 and 3 it has been assumed for the sake of making a comparison between the values for normal bone

7. Wyatt, T. C., and McEachern, T. H.: Congenital Bone Dysplasia (Osteogenesis Imperfecta) Associated with Lesions of the Parathyroid Glands, Am. J. Dis. Child. **43**:403 (Feb.) 1932.

and those for bone from patients with osteogenesis imperfecta that the samples were uniform. This, we admit, may be misleading since we had no way of determining in several instances just what part of the bone or how much was used for analysis. We are certain that the more cartilage is included in the specimen the higher will be the sodium and potassium content of the bone ash. The specimen used in our study was cut from the shaft of the femur, and about 1.5 Gm. of bone was taken for analysis.

The deviations from the norm observed in table 1 may serve to indicate the pathologic metabolism in osteogenesis imperfecta. Apparently

TABLE 2.—*Analysis of Normal Bone Compared With That of Bone from Patients with Osteogenesis Imperfecta*

Condition of Infant	Dry Bone, Gm.	Total Ash		Calcium*	Magnesium	Phosphorus	Potassium	Sodium	Author
		Gm.	Percentage of Dry Bone						
Normal.....	1	.....	....	5.01	0.12	2.93	....	....	Howland, Marriott and Kramer: J. Biol. Chem. **68**: 721, 1926
Normal.....	1	0.608	60.8	5.61	0.12	3.04	....	0.14	Sindler
Osteogenesis imperfecta	1	0.415	41.5	2.46	0.37	2.90	0.41	1.96	Sindler
Osteogenesis imperfecta	1	0.452	45.3	4.24	0.11	2.83	0.16	0.10	Swanson and Iob

* The values for the minerals are expressed in millimols per gram of dry bone.

TABLE 3.—*Percentage Composition of Normal Bone Compared With That of Bone from Patients with Osteogenesis Imperfecta*

Condition of Infant	Author	Ash, Percentage	Percentage Composition of Ash				
			Calcium	Magnesium	Phosphorus	Potassium	Sodium
Normal.....	Sindler.....	60.8	37.0	0.53	15.5	....	0.53
Normal.....	Wyatt and McEachern....	....	35.3	....	17.9	....	0.84
Osteogenesis imperfecta	Sindler.....	41.5	23.8	2.36	21.8	3.89	10.86
Osteogenesis imperfecta	Wyatt and McEachern....	....	34.2	....	16.7	....	1.21
Osteogenesis imperfecta	Swanson and Iob.....	45.2	37.6	0.66	19.4	1.41	0.52

a better retention of calcium and phosphorus results during the time of administration of calcium citrate [4] or calcium lactate.[2] Obviously many physicians may have given cod liver oil or viosterol to infants with this disease, but no metabolism experiments have been reported. The infant in our study received 30 drops of viosterol daily. This dose caused no marked improvement but a consistent and satisfactory retention of both calcium and phosphorus. The values for the other minerals determined showed marked fluctuation, and in the last period the values for sodium showed a negative balance. Feeding experiments on rats have convinced us that viosterol in therapeutic and even in much larger doses does not

influence the retention of sodium, potassium or chlorine. On the whole the retention of calcium and phosphorus seems to be sufficient for good skeletal growth, so if this disease were only a derangement of the bone-forming tissues growth approaching the normal should have resulted. However, there must be some additional limiting factor since our patient gained about 570 Gm. in three months. There is as much evidence in our summarized data to indicate that not only is there an impairment of mineral utilization by the skeletal tissues but other body tissues and tissue fluids may be suffering from a disturbed mineral balance which prevents normal growth. The low retention of sodium and to a lesser extent of potassium and chlorine supports the conclusion that osteogenesis imperfecta is not only a skeletal disturbance but a more inclusive derangement in which the entire mineral metabolism may be primarily or secondarily involved.

CONCLUSIONS

A table has been compiled to show the available data on the mineral metabolism in osteogenesis imperfecta. Additional data on the case of a patient fed 30 drops of viosterol daily have been included. There is some indication that viosterol improves the calcium and phosphorus retention.

The most striking finding is the poor retention of sodium in patients with osteogenesis imperfecta.

The results of analyses of bone from a patient with osteogenesis imperfecta have also been included. Our observations show the low total ash content of the bone that has been reported in the literature but do not confirm the high values reported for magnesium, sodium and potassium.

Case Reports

ALBERS-SCHÖNBERG'S DISEASE

J. HAROLD ROOT, M.D.
WATERBURY, CONN.

The condition known as marble bones was first described by Albers-Schönberg [1] in 1904 and is usually referred to by his name. It is also called osteopetrosis and congenital osteosclerosis. Karshner [2] gave a complete review of the literature to 1926, finding eighteen reported cases and adding four of his own. Mayer and Pitts,[3] in 1933, referred to seventeen additional cases and reported one more. Since 1926 thirty cases have been reported in the literature in addition to those mentioned by Mayer and Pitts, making a total of seventy cases up to 1933. Thirty-five, or one half, of the reports have appeared in the past five years, showing that the condition either is more prevalent than was once supposed or is recognized more frequently.

REPORT OF A CASE

The following case is presented in order to bring forward again the typical picture of this rather uncommon disease.

Mary D. was admitted to the Waterbury Hospital on March 13, 1933, at the age of 6 weeks, with the complaint of cough for about a week, crying and failure to gain weight.

The mother and father were both 24 years old and well. One sister, 14 months old, was well. No miscarriages or deaths had occurred. Roentgen ray examination of the parents and sibling showed normal bones. There was no history of a disease of the bones in the family. The child's father was the mother's uncle. The baby was born at the Waterbury Hospital at full term. Delivery was normal. The physical examination revealed no abnormalities, and she was discharged on the ninth day in apparently good condition. There was no gain in weight from the time the infant was 2 weeks old. She was weaned from the breast shortly after leaving the hospital and cried a great deal subsequently. A cough developed a week before the last admission.

Physical examination on admission revealed a poorly nourished infant with a distended tympanitic abdomen, medium moist râles at the base of each lung, a

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From the Pediatric Service of the Waterbury Hospital.

1. Albers-Schönberg, H. E.: Röntgenbilder einer seltenen Knochenerkrankung, München. med. Wchnschr. **51**:365, 1904.

2. Karshner, R. G.: Osteopetrosis, Am. J. Roentgenol. **16**:405, 1926.

3. Mayer, O. B., and Pitts, T. A.: Osteopetrosis, J. A. M. A. **101**:22 (July 1) 1933.

dull red, bulging left ear drum and some redness of the right ear drum. Otherwise the observations were essentially normal. The liver and spleen were not palpable. There was no strabismus or nystagmus; the eyegrounds showed slight pallor.

A formula of evaporated milk and dextrose was taken well by the infant, and cod liver oil, 1 drachm (3.69 cc.), and orange juice, ½ ounce (14.8 cc.), were given each day. A satisfactory gain in weight occurred except as interrupted by otitis media and other infections. On April 1 an inflammation developed in the left side of the lower gum which cleared up after several days. Two days later cellulitis appeared over the left side and midpart of the lower jaw extending to the cheek and neck. On April 6 an incision was made just under the chin, and a large

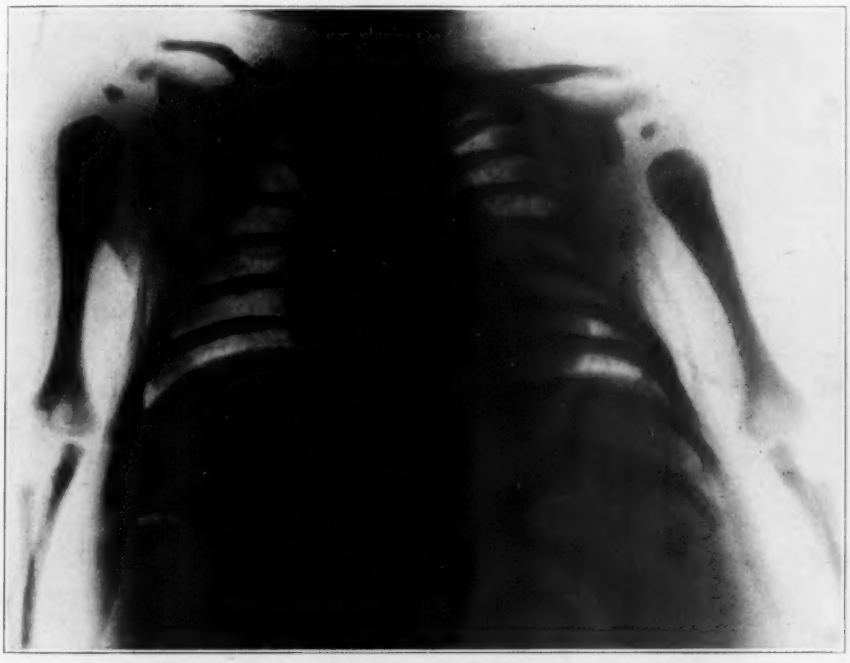

Fig. 1.—A recent fracture of the upper part of the right humerus with a beginning callous formation is shown, as well as an old fracture of the upper part of the left humerus. There is marked increased density of all the bones (April 4, 1933).

amount of pus was evacuated. A roentgenogram of the jaw at this time showed no evidence of change in the mandible. On April 17, however, an involucrum was shown below the mandible on the left side, with some destruction of the mandible proper. A diagnosis of osteomyelitis was made.

On April 24 it was noticed that the right arm was not moved and that touching it caused pain. A recent fracture of the humerus was demonstrated by roentgenograms, and at this time greatly increased density of all the bones was discovered. Fractures were found in the upper part of both humeri, the upper part of the left femur, the middle of the right femur and the middle of both tibias. A large amount of callus was present about the fractures, most marked at the most recent

fracture of the right humerus. All the fractures had united in good position and in alinement. The normal osseous markings were obliterated throughout the skeleton. A thin layer of calcium was seen under the periosteum about both femurs and both tibias. There was a marked band of lesser density near the ends of all the long bones. The disease appeared to be well advanced, and probably

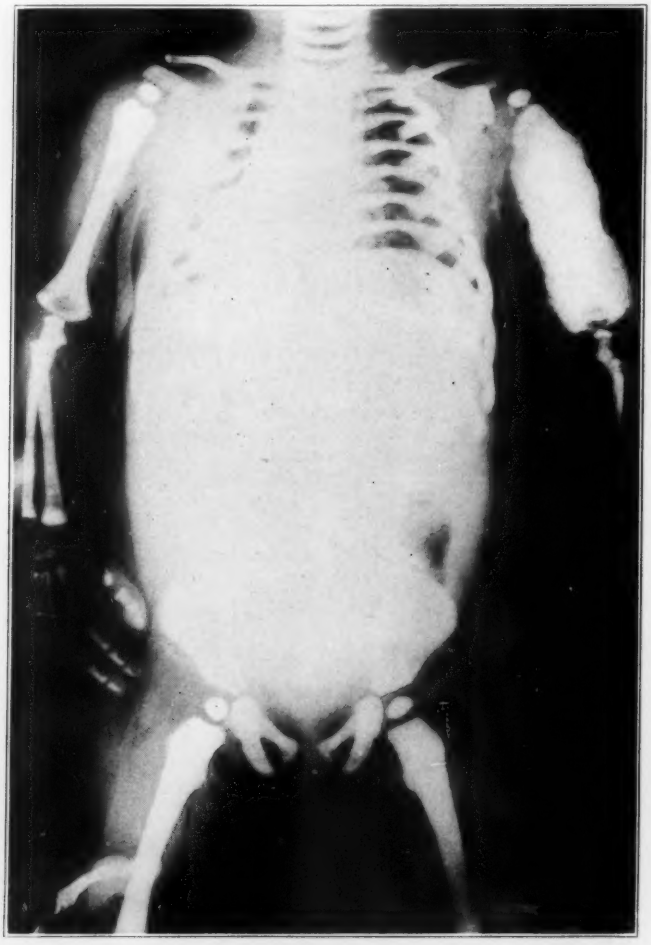

Fig. 2.—The appearance of the right humerus is shown ten months after the fracture and six months after the removal of a piece of callus. There is marked density of all the bones, with the normal markings obliterated. There are bands of decreased density at the ends of the long bones and a similar band in both iliac bones (Feb. 2, 1934).

the old healed fractures occurred in utero. No transverse or longitudinal bands and no clubbing of the ends of the long bones could be demonstrated. Swelling and tenderness of the upper part of the right arm continued to be pronounced until discharge from the hospital on May 13. A roentgenogram of the right arm on

April 28 showed an enormous amount of callus around the entire shaft of the right humerus, the callus on each side being greater in width than the humerus (fig. 1). Extensive swelling of the soft tissues of the entire arm and shoulder was present. The excessive callous formation was thought to be due to a calcified subperiosteal hemorrhage.

Laboratory examination on April 27 revealed: blood calcium, 11 mg. per hundred cubic centimeters, and blood phosphorus, 5 mg. On June 7 the blood calcium was 9 mg. and the blood phosphorus, 5 mg. On March 13 the reaction to the Mantoux test was negative with 0.1 mg. of tuberculin. The urine was consistently normal except for an occasional slightest possible trace of albumin. The reaction to the Kahn test was negative on April 24. The mother's reaction to the Wassermann test was negative in November 1932 when she was eight months pregnant.

In August 1933, when the infant was 7 months old, a piece of bone was removed from the right humerus by Dr. W. M. Verdi, Hospital of St. Raphael, New

Blood Counts for Patient with Albers-Schönberg's Disease

	3/13/33	5/2/33	6/5/33	9/2/33	9/5/33	2/2/34
Hemoglobin*.....	75%	70%	64%	40%	50%	65%
Erythrocytes.....	3,400,000	3,600,000	3,500,000	2,000,000	2,600,000	3,700,000
Leukocytes.....	15,600	22,200	11,100	10,000	12,800	12,800
Neutrophils.....	20%	35%	43%	67%	68%	21%
Mononuclears.....	26%	12%	....	....	....	4%
Lymphocytes.....	46%	50%	50%	30%	30%	70%
Myelocytes.....	8%	....	....	....	....	....
Eosinophils.....	...	3%	5%	....	....	3%
Endothelial cells....	...	...	...	....	....	2%
Transitionals.....	...	...	...	3%	....	...
Basophils.....	...	...	...	...	2%	...
Reticulocytes.....	...	...	...	...	...	4%

* The hemoglobin concentration was estimated by the Sahli technic, in which the normal value is 17 Gm. per hundred cubic centimeters.

Haven, Conn. The bone was described as crumbly and soft. Microscopic examination by Dr. J. O. Collins at the Waterbury Hospital revealed normal callus.

At the age of 9 months physical examination revealed a pale, fairly well nourished baby. One midincisor was erupted in the upper jaw. The liver was palpable two fingerbreadths below the costal margin and the spleen one fingerbreadth below the margin. Lateral nystagmus was present, and the head was thought to be enlarging.

At the age of 1 year the baby was pale and undersized and showed a moderate degree of hydrocephalus. Its length was 26½ inches (67.31 cm.). The circumference of the head was 17½ inches (44.45 cm.), and that of the chest, 16 inches (40.64 cm.). The fontanel was open to the width of three fingers. There were lateral nystagmus and external strabismus of the right eye. The liver was palpable three fingerbreadths below the costal margin and the spleen one fingerbreadth. There were optic atrophy and complete loss of vision. Three upper incisors were present and one lower molar on the left. The child was unable to sit alone. Roentgenographic examination revealed that the bands of relatively less density at the

ends of the bones of the extremities had increased in width. They evidently represented areas of growth. A similar band was seen in both iliac bones. Periosteal elevation was present. The right humerus still showed marked deposits of calcium about 4 cm. in diameter, involving practically the whole bone. All the bones were even more dense than formerly, and there was clubbing of the lower ends of the femurs (fig. 3).

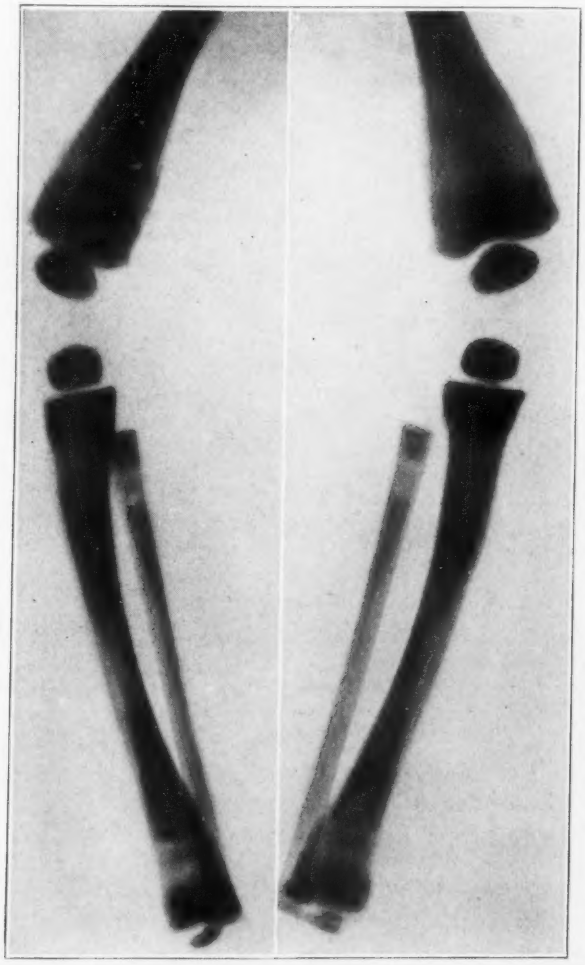

Fig. 3.—The bones of the lower extremities at the age of 1 year are shown. There are bands of lesser density at the ends of the bones and beginning clubbing of the lower ends of the femurs (Feb. 2, 1934).

COMMENT

Marble bones is a familial, hereditary, congenital disease. Several instances have been reported in which the disease occurred in more than one child of the same family as well as in one parent. Cases have

also been reported in cousins. The disease occurs in the fetus (Pirie).[4] The oldest patient in whom it has been reported was 58 years old (Zadek).[5] Inbreeding is a factor in the cause of the disease. Some relationship has been reported in the parents of most of the patients, particularly in some of the cases more recently reported. Various theories as to the etiology of the condition have been advanced, but no proof in support of any one theory has been offered. The most popular theory at present is that the calcium metabolism is faulty, perhaps secondary to glandular dysfunction, particularly disturbances of the parathyroid bodies. The bony changes are variously accounted for under this theory. The most logical explanation is that the blood tends to maintain a constant calcium level; calcium is excreted through the kidneys or is deposited in the tissue, and there is simultaneously a rarefaction of bone in some areas and condensation in others; in marble bones this process is accentuated and out of balance. Sick,[6] Laurell and Wallgren,[7] Lorey,[8] D'Istria[9] and Péhu, Policard and Dufourt[10] are the chief exponents of this view. Guassardo[11] suggested an abnormal neuro-endocrinologic innervation, causing the bony changes through faulty calcium metabolism. Ghormley,[12] Kopylow and Runowa,[13] Kudrjawtzewa[14] and Llado[15] expressed the opinion that a high blood phosphorus content may be of etiologic importance. The endocrine system may play a part in the phosphoremia, which in turn causes marble bones.

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Pirie [4] observed the development of marble bones in three siblings. He suggested that the disease is an infection starting at the epiphyseal line and spreading to the medulla and that it is closely related to rickets. Schulze [16] considered the condition to be a rachitic osteomalacic process. Windholz [17] suggested a relation between marble bones and leukemia, and, more recently, Robertson [18] offered some evidence to link the condition with Cooley's anemia.

PATHOLOGIC PROCESS

There are few descriptions in the literature of the microscopic osseous picture in this condition. Nadolny [19] described microscopic evidence of building of bone. He found the zone of ossification to be irregular and broadened in the epiphyseal cartilage, with profound disturbance of calcification of the cartilage ground substance. The medullary portion of the cartilaginous epiphysis presented extensive calcification. In the adjacent bone medulla the cartilage cells were not properly demolished, leaving an irregular persistence of excess cartilage ground substance. Except for the disturbance of ossification no abnormality was noted in the cartilage.

Pirie [4] described the epiphysis as showing relatively normal-appearing cancellous bone composed of spicules with little enclosed cartilage. The histologic structure of the diaphysis, according to Pirie, is distinctly different from that of the epiphysis. It impressed him as being fundamentally calcified cartilage in which are smaller and irregular open spaces. The open areas compose less than 25 per cent of the total structure and are lined with irregular masses of bony tissue. Scattered throughout the calcified cartilaginous material and completely surrounded by it so that no open space is present are innumerable small spherical foci of ossification. Flattened osteoblasts are conspicuous about the lining spaces, but typical osteoclasts are comparatively rare. He said that entering the shaft the ossification is much more complete, open spaces are much larger, and myeloid cells are found in them. Nevertheless even here an abnormal amount of cartilage is present in the bony spicules and there is a relatively large amount of osteoid tissue. A definite zone of compact bone of considerable thickness is present beneath the periosteum.

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SYMPTOMS

The outstanding features of the disease are extreme density of the bones with obliteration of the normal markings and a tendency, particularly of the long bones, to fracture. The fractures occur at right angles to the shaft. According to some authors, they are due to a decrease in elasticity because of an abnormal deposit of calcium; others say that the fractures occur because of abnormal fragility at the points of the transverse bands of lesser density. The fractures in young patients tend to heal rapidly with a large callous formation, but in older patients the fractures heal more slowly or not at all. Transverse bands are commonly seen in the long bones, compared by some to the annual rings of trees. Often longitudinal striations are found. Frequently there is marked clubbing of the ends of the long bones, most marked at first where the growth of bone is most rapid, as at both ends of the femur, the upper end of the humerus and both ends of the tibia and fibula. All the bones are involved, and the process is most evident in the bodies of the vertebrae, in the central portion of the pelvis, at the base of the skull and at the ends of the long bones. The posterior clinoid process is usually thickened.

Hydrocephalus is common, and, owing to pressure on the cranial nerves caused by narrowing of the bony canals, there are often nystagmus, strabismus and optic atrophy. Partial or complete blindness may result. Occasionally deafness is encountered. Interference with dentition is a common observation, and necrosis of the lower jaw has been reported frequently. Anemia is a constant observation in later stages of the disease because of interference with the function of the marrow by encroaching bones.

The liver and spleen are usually enlarged, and general glandular enlargement has been reported in the more severe cases and in cases with anemia. The mentality is normal unless hydrocephalus is present. Physical development is often retarded. The teeth appear late and become carious early. Sitting up, walking and talking are delayed.

The course of the disease is extremely variable, and the severity depends on the secondary characteristics. There is almost complete sclerosis in some cases in which little anemia is present and there is only slight enlargement of the liver, spleen and lymph glands. In other cases there is little sclerosis, with marked anemia and marked enlargement of the liver, spleen and lymph glands. The severe forms in childhood are fatal, and the most severe forms may cause death in utero or soon after birth. Patients with less severe forms may live to middle life. In general, the later in life the disease manifests itself the more chronic it becomes and the more hopeful the outlook.

The blood calcium level has been normal in most cases in which the calcium content was examined. A number of observers have

reported an increase in the blood phosphorus content, while others have reported a normal value. Pirie demonstrated that the bones cut like chalk rather than like marble and that the density is due to deposits of calcium carbonate. He gave the calcium content of marble bones as 29.2 per cent, the normal being from 28 to 29 per cent by weight, but said that the calcium is, of course, much increased by volume. Kopylow and Runowa gave the calcium content of normal bones as 24.31 per cent, that of marble bones as 29.94 per cent, and that of rachitic bones as 21.30 per cent. Kudrjawtzewa gave the calcium content of normal bones as 28.8 per cent, and that of marble bones as 29 per cent.

No treatment has been of benefit in this condition. The administration of parathyroid extract has been tried in several cases, the most recent report being that of McCune and Bradley,[20] with failure to obtain a negative balance.

CONCLUSION

There were several unusual features in the case reported here. Six fractures, one fresh and five old healed ones, were found when the disease was first recognized, the patient being 10 weeks old. Some fractures must have occurred in utero. The degree of anemia, of enlargement of the liver and of other secondary characteristics of the disease were very slight compared with the marked sclerosis presented by the bones. The course of the disease was much slower and less severe than ordinarily occurs when there is such a degree of involvement of the bones at this early age. The tremendous callous formation at the site of the most recent fracture in the right humerus was of interest. A piece of bone removed from the callus proved to be soft and crumbly, and microscopic examination revealed the characteristics of normal callous formation.

SUMMARY

A case of Albers-Schönberg's disease, or marble bones, is presented in detail.

Seventy cases have been reported in the literature.[21] Some of the interesting points about the cases are reviewed, and the pathologic

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process and symptomatology are discussed. Opinions as to the etiology of the condition fall into the following groups: (1) faulty calcium metabolism secondary to endocrine imbalance; (2) faulty phosphorus metabolism, also secondary to endocrine imbalance; (3) infection; (4) a rachitic osteomalacic process, and (5) a leukemic condition.

The case presented showed some unique features, the outstanding ones being the huge callous formation at the site of the most recent fracture and the mildness of the secondary symptoms in comparison with the marked sclerosis of the bones.

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PERSISTENT CONGENITAL ATELECTASIS

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CHICAGO

Persistent congenital atelectasis in older infants is an interesting and comparatively rare condition, and for that reason the following report of a case is warranted.

REPORT OF A CASE

History.—B. C., a girl, aged 11 weeks, was first seen at home on April 29, 1932. The infant was born at a hospital on February 11, at full term, and weighed 6 pounds and 8 ounces (2,948.34 Gm.) at birth. The birth was normal in all respects. During the first six days of life the baby did not nurse well, and during the first month of life she was unusually drowsy and had frequent cyanotic spells. The attending physician, who examined her frequently, diagnosed the condition as possible involvement of the thymus but ordered no roentgenograms or treatment of any kind to relieve the cyanosis. During the second month of life the baby improved; she ate well, and the cyanotic spells disappeared. She continued to thrive until April 27, when she began to cough and to have difficulty in breathing. She had a slight rise in temperature, was restless and did not sleep well. The cough became worse, and on April 28 she began to have cyanotic spells again.

Examination.—When first seen the infant looked acutely ill. The temperature was 100.6 F. rectally. She had marked dyspnea with wheezing respiration, and there was retraction of the costal margins. The impression obtained at first glance was that the infant had severe asthmatic bronchitis or bronchial asthma.

However, on examination of the chest, definite suppression of breath sounds was noted over the upper lobe of the right lung, with impairment of resonance over that area; there was suppression to absence of breath sounds over the apex of the left lung, and many whistling râles, chiefly expiratory, were noted over the remaining parts of both lungs.

The heart was displaced to the right. The right border of the heart was about 1 cm. to the right of the sternum, and the left border was well inside the nipple line. The abdomen was distended. Further examination gave essentially irrelevant results.

Owing to the marked findings in the chest the baby was removed to the Children's Memorial Hospital for further examinations and study.

Course.—During the first day in the hospital the wheezing became worse, and marked cyanosis of the lips was noted. The response to treatment with solutions of epinephrine hydrochloride was slow. The patient was placed in an oxygen tent, where her respirations became easier and her color improved.

Dr. Joseph Brenneman examined the infant on April 30 and made the following notation: "The child is very sick. She has a definite asthmatic wheeze. There is suppression of breathing over both lungs, especially over the apex of the left

lung. The heart is displaced to the right. The left lung is either displaced by a cyst or markedly emphysematous, so that it extends far to the right of the sternum."

Toward night of the same day the child became more dyspneic; the wheezing increased, and the cyanosis became more marked. Solution of epinehprine hydrochloride given frequently yielded no relief. Oxygen and carbon dioxide were of no value. She became progressively worse and died at 1:15 a. m., about twenty-eight hours after admission. The terminal temperature was 105 F.

Laboratory Examination.—Blood: The hemoglobin was 78 per cent; the red cells, 5,000,000; the white cells, 7,000, with 47 per cent polymorphonuclears, 52 per cent lymphocytes and 1 per cent monocytes.

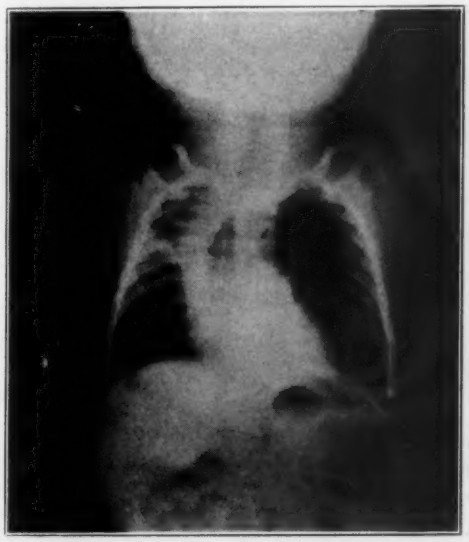

Fig. 1.—Roentgenogram showing partial obliteration of the upper half of the right pulmonary field with deviation of the mediastinal structures and trachea to the right and marked compensatory emphysema of the upper two thirds of the left pulmonary field.

Urine: The urine was entirely normal.

Roentgenographic Examination (by Dr. W. E. Anspach).—First Examination (April 30): Several roentgenograms were made during life in an effort to explain the unusual zone of decreased density which extended from the upper part of the left lung to beyond the spine on the right side. There was partial obliteration of the upper half of the right pulmonary field with deviation of the mediastinal structures and trachea to the right (fig. 1). There was marked hyperaeration of the left pulmonary field, especially of the upper two thirds (compensatory emphysema). It was believed that the shadow of decreased density on the upper part of the thoracic portion of the spine was explainable by this process. The heart was slightly displaced to the right but apparently not enlarged. Roent-

genograms of a lateral view (fig. 2) failed to add information, except that there was a triangular area of increased density in the costophrenic angle posteriorly (atelectasis).

Postmortem Examination (May 1, 1932): The general appearance (fig. 3) was unchanged from that observed in previous roentgenograms except that there was considerably more displacement of the mediastinal structures to the right and markedly increased compensatory emphysema of the left lung. One would almost expect emphysematous bullae or marked bleaching of the tissues at necropsy. There was a partial clouding of the left cardiohepatic angle.

Partial atelectasis of the upper lobe of the right lung and atelectasis of the upper portion of the inner thirds of the remaining two lobes were observed (fig. 4).

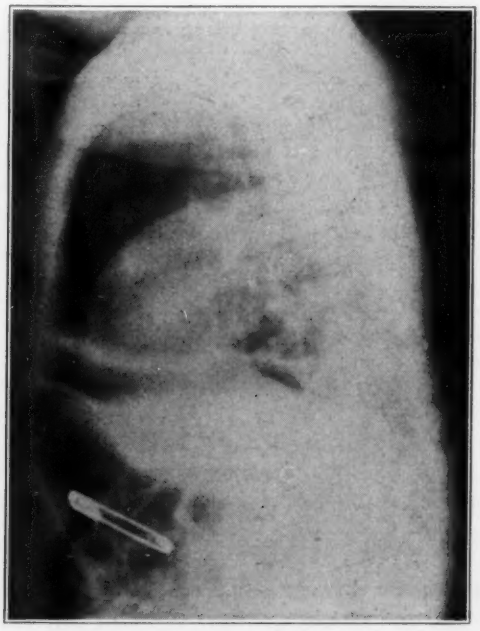

Fig. 2.—Lateral view roentgenogram, showing a triangular area of increased density in the costophrenic angle posteriorly (atelectasis).

The left lung showed marked ballooning of the alveoli, evidenced by the wide space between the bronchovascular markings and the "lacelike" appearance of the tissue. The lower lobe of the left lung was apparently completely atelectatic.

Roentgenograms of the femurs showed a slight flaring but practically no evidence of rickets.

Impression: The diagnosis was (1) atelectasis of the upper lobe of the right and the lower lobe of the left lung and (2) high grade compensatory emphysema of the upper lobe of the left lung which had extended beyond the spine to the right.

Autopsy (by Dr. I. J. Wolman).—The body was that of a well developed and well nourished white female infant weighing 9 pounds (4,082.33 Gm.) and measuring 57 cm. in length. The skin had a good color and turgor; it showed no abnormalities except for a mark made by a needle puncture in each thigh. Jaundice

Fig. 3.—Postmortem roentgenogram showing a picture similar to that presented in figure 1, with considerably more displacement of the mediastinal structures to the right and markedly increased compensatory emphysema of the left lung.

Fig. 4.—Postmortem roentgenogram of specimen showing partial atelectasis of the upper lobe of the right lung and atelectasis of the upper inner thirds of the remaining two lobes. The left lung shows marked ballooning of the alveoli, evidenced by the wide space between the bronchovascular markings and the "lacelike" appearance of the tissue. The lower lobe of the left lung is apparently completely atelectatic.

and cyanosis were not evident. There was no discharge from the ears, eyes or nose. The conjunctivae and pupils seemed normal. The mouth was clean. The cervical and other superficial lymph nodes were not palpable. The thorax was abnormally rounded, almost barrel-shaped. Its transverse diameter was 12 cm., and its anteroposterior diameter, 9 cm. The abdomen was not distended. The umbilicus appeared normal. The external genitals presented no discharge. The extremities were not remarkable.

Sectioning was restricted to the trunk, which was opened through the usual crossbow incision. There was a moderate amount of subcutaneous pale fat, and the tissues did not appear dehydrated. No anatomic anomaly was found.

Abdominal Cavity: The peritoneal surfaces were smooth, pale and glistening and free from adhesions and exudate.

The liver was somewhat enlarged, extending two fingerbreadths below the right costal margin. The capsule and gallbladder were not remarkable. The parenchyma was reddish tan, and blood oozed freely from the surface made by cutting. The individual lobulations appeared a little swollen and were definitely yellow.

The spleen weighed 13 Gm., and its capsule was free from adhesions. The parenchyma was moist and dark red and did not rise above the cut edge of the capsule. The malpighian bodies were not evident. The pulp could not be scraped away with a knife.

The suprarenal glands and pancreas showed no special changes.

The kidneys were similar in appearance and practically normal. They were somewhat congested. The internal architecture was not distorted. The pelves and ureters were not dilated and had a smooth white lining. The bladder was not abnormal. The internal genitals were of the usual female type.

Gastro-Intestinal Tract: The stomach contained some milky fluid. There were no hemorrhages in its lining. The small and large intestines contained food in the process of digestion. The feces in the large bowel were semisolid and yellow. There were no ulcerations or other lesions of the mucosa. The mesenteric lymph nodes were not swollen but were a little hyperemic. The diaphragm was intact; its level was not noted.

Thoracic Cavity: The thoracic cage seemed unusually well arched anteriorly, and the sternum with the contiguous costocartilages had a dome-shaped contour. The centers of ossification in the sternum were very small. The thoracic organs presented an unusual appearance. The anterior portion of the left lung extended over the front of the heart so that its edge lay 2 cm. beyond the midline; it was pale pink and emphysematous. The upper margin displaced the lower part of the thymus laterally to the right. The pericardium and the heart were displaced posteriorly behind this anterior lappet of the left lung, which was 3 cm. in thickness in this region. The right lung was visible only to a slight extent and appeared grayish red. There were no adhesions, air or exudate in either pleural cavity. The relative positions of these organs was well shown in the roentgenograms taken after death.

Each lung weighed 50 Gm. The upper lobe of the left lung was hyperdistended with air. Its individual vesicles could be recognized beneath the pleura; they had an average width of slightly less than 1 mm. The distention appeared a little more marked in the anterior half of the lobe. The tissue was pale pink and crepitant throughout. No depressions were noted on the surfaces, and no consolidations could be palpated within its substance. The lower lobe of the left lung was almost but not entirely separate from the upper lobe. This lobe was reddish purple and very small, measuring only 4 by 3.5 by 3.5 cm. It had a normal shape, however. It was collapsed and airless; the bronchi were not dilated and appeared

empty. It lay tucked away behind the extremely emphysematous upper lobe, which almost entirely filled that half of the thorax.

The right lung was reddish gray and had a smooth, irregular outer surface. It was crepitant throughout, more so in the anterior than in the posterior portions. It appeared to be in a state of partial collapse. No zones of complete atelectasis or consolidation were found. There were a few petechiae in the pleura.

When placed in water, the right lung floated, though almost completely submerged. The lower lobe of the left lung sank. The emphysematous upper lobe rested lightly on the surface of the water. (The lungs are preserved in the museum.)

The pericardial sac was not dilated and contained about 3 cc. of clear, straw-colored fluid. The surface was smooth and pale. The heart was not dilated and

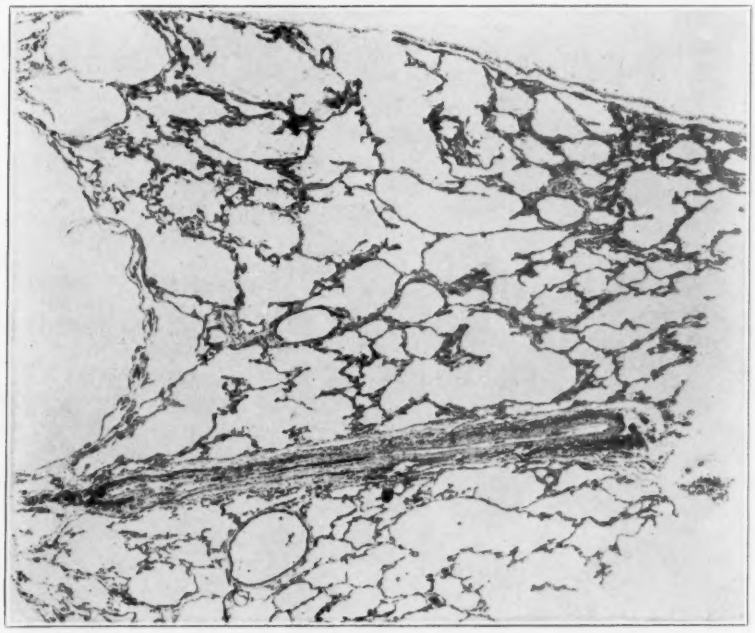

Fig. 5.—Photomicrograph of tissue of the upper lobe of the left lung, showing a marked degree of emphysema, with enormously distended alveoli and much thinned and in places ruptured alveolar walls; a single dilated bronchiole is also included.

had the usual size and appearance. It weighed 20 Gm. The ductus arteriosus was closed. The myocardium was somewhat pale and firm. The valves were normal. The foramen ovale was almost completely obliterated by a delicate valve, the edge of which had not fused.

The thymus was pink and fleshy. It weighed 6 Gm. and did not seem markedly atrophic. It extended about 2 cm. below the base of the heart.

The line of ossification of the ribs was straight and regular. The skull and cranial contents were not examined.

Microscopic Examination: There were two sections of pulmonary tissue. The first, taken from the upper lobe of the left lung, showed a marked degree of

emphysema, with enormously distended alveoli and much thinned and in places ruptured alveolar walls. A single bronchiole, also dilated, was included in the section (fig. 5).

The second showed widespread atelectasis. The air spaces were narrowed, and in places their walls were completely collapsed and almost touching. The alveolar capillaries were filled with blood. The bronchioles were lined with their normal epithelium, and their lumens contained a small amount of mucoid débris (fig. 6).

Bacteriologic Report: Cultures of blood from the heart showed bacilli of the colon group, Staphylococcus albus and a few pairs and chains of gram-positive cocci which were not isolated for identification.

Postmortem Diagnosis: The diagnosis was congenital atelectasis of the lower lobe of the left lung, extreme compensatory emphysema of the upper lobe of the

Fig. 6.—Photomicrograph of atelectatic tissue. The air spaces are narrowed, their walls in places completely collapsed and almost touching. The alveolar capillaries are filled with blood. The bronchioles are lined with normal epithelium, and their lumens contain mucoid débris.

left lung, acute tracheobronchitis, compression atelectasis of the entire right lung, displacement of the heart and mediastinum to the right and circulatory congestion of the liver, spleen and kidneys.

COMMENT

The scarcity of literature on persistent congenital atelectasis is rather striking. The modern textbooks on pediatrics describe congenital atelectasis of the new-born in detail, but with few exceptions, they do not mention persistent congenital atelectasis or they say but little regarding the condition.

Morse [1] in discussing congenital atelectasis stated that an infant may live for a few days or weeks, showing no symptoms except feebleness, and then die suddenly. In such cases autopsy reveals atelectasis of the lungs.

Sheffield,[2] in his textbook, mentioned only the fact that infants with congenital atelectasis may live for weeks or months.

Rommel,[3] in writing for Pfaundler and Schlossmann's work, made the following statement: "Now and then asphyxia occurs, especially in premature children, as late as a few weeks after birth and is then usually a bad sign."

Pearce,[4] in Abt's work on pediatrics, said: "Many times in infants several weeks of age who have died from some unallied cause, and have shown no signs of cyanosis or respiratory distress, postmortem examination has shown as much as two thirds of the lungs to be in a state of atelectasis."

Holt and his co-worker,[5] in discussing atelectasis of the new-born, stated that on several occasions they had seen cases in which there was nothing to attract attention to the lungs until the final attack of cyanosis occurred. To illustrate this point they described in detail the following 2 cases:

> The infants were twins, aged 10 weeks, and delicate. Suddenly at night one child was taken with convulsions, became deeply cyanotic and died in two and one-half hours. He had been suffering from a slight attack of indigestion for a week previously. The other twin had been apparently well on the previous day. Two hours after the death of the first child the second was taken with similar symptoms and died in a few hours. At autopsy there was found extensive atelectasis involving the posterior part of the upper and the greater part of both lower lobes. The lesions were almost identical in the two children.

Ruhräh [6] reported the case of a child aged 4 months with cyanosis, clubbing of the fingers and toes and dilatation of the superficial veins of the chest in whom there were no physical signs of involvement of the heart and lungs. The roentgenograms revealed disseminated patches of unexpanded pulmonary areas varying in size from that of a pinpoint

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to that of a grain of wheat, scattered throughout both lungs, more numerous in the left and more sparingly distributed in the outer portion of each lung. When the child was 2 years of age the clinical and roentgen findings were normal.

Cohen [7] mentioned the fact that congenital atelectasis may persist for several months.

Rose [8] described in detail 2 cases of persistent congenital atelectasis. He was interested in these cases from the roentgenologic standpoint and stated that the literature on roentgenology in connection with this subject is very scarce.

The first case was that of a premature infant who entered the hospital when 4 weeks of age, with a cold and dry cough of a week's duration. The physical examination showed no definite impairment of resonance, although fine and coarse crackling râles were heard over the base of each lung and at the angle of each scapula posteriorly. These findings continued almost unchanged during the rest of the child's life. During the last ten days repeated attacks of cyanosis occurred, and stimulants, oxygen and carbon dioxide and artificial respiration were used. The child died at 2 months of age. The roentgenograms showed a disseminated infiltration in the mesial portion of each lung and a clear periphery.

The second was that of a premature infant who was cyanotic at birth and had attacks of cyanosis for the first ten days of life. The infant was kept in the hospital for three months and showed a slow gain in weight. During the following three months at home the child gained fairly well but was troubled with colds and coughs. At 6 months of age the child was readmitted to the hospital, as there was difficulty in feeding him. For the next three months the condition remained substantially the same. The cough persisted. On physical examination little change was noted from week to week. The lower lobe of the right lung was definitely dull, with bronchial breathing and a few crepitant and subcrepitant râles. The left lung showed definite bronchovesicular breathing. The clinical diagnosis was that of unresolved pneumonia. There were terminal furunculosis and bilateral otitis media, and death occurred at 9 months. The roentgenograms showed considerable intensification of the pulmonary markings and small disseminated patches of consolidation heavier near each hilus, with the peripheral portion of each lung almost clear.

Postmortem examination was made on each child, and the observations were similar in the two cases. Fetal atelectasis was noted in the dorsal half of the upper lobe of the right lung. Ninety per cent of the lower lobe of the right and 75 per cent of the lower lobe of the left lung were solid.

In contrast to the scarcity of cases of persistent congenital atelectasis is the frequency of atelectasis in the new-born.

In order to prevent the occurrence of these unusual cases of persistent atelectasis it is important that physicians be able to recognize the condition early and to give the proper treatment for atelectasis occurring in new-born infants. All cases of cyanosis in new-born infants

7. Cohen, S. A.: Congenital Atelectasis, Boston M. & S. J. **85**:374 (Sept. 29) 1921.

8. Rose, C. B.: Persistent Congenital Atelectasis, Radiology **14**:488 (May) 1930.

require a careful study, and roentgenograms of the chest should be taken. Only by roentgen study can these cases be definitely diagnosed.

Davis and Stevens,[9] in a study based on a routine roentgenographic examination of a series of 702 infants, stated that an abnormal pulmonary condition was found in 184, or in 26 per cent. Poor aeration of the lungs was noted in 38 and atelectasis in 84 infants.

Epstein,[10] in reviewing 1,000 consecutive necropsies, stated that atelectasis was the cause of death in 8 cases. Four of these cases occurred in the first month of life, and 4 occurred between the first and the twelfth month. He also stated that atelectasis was noted in 27 cases in which deaths occurred from other causes.

Hunt,[11] in examining 118 infants who showed cyanosis, found gross atelectasis in 39. He stated that in most instances it was of little importance. In 4 cases, however, it was severe, involving the major part of one or more lobes. In each of these cases there was also a large cerebral hemorrhage which was probably the primary lesion and the cause of the cyanosis.

Dunham [12] reported 6 cases of congenital atelectasis in the newborn and emphasized that the main symptom is cyanosis, and that by means of roentgenograms this cyanosis can be differentiated from cyanosis caused by other conditions.

CONCLUSION

In the case reported here the infant showed definite cyanosis shortly after birth and continued to have cyanotic spells during the first month of life. No roentgenograms of the chest were taken. As a result a proper diagnosis of congenital atelectasis was not made and no treatment to correct that condition was given.

The treatment consists of inhalations of a mixture of from 5 to 10 per cent carbon dioxide and oxygen. This has been advocated by Henderson [13] and his co-workers. It has proved to be of great value. It

9. Davis, C. H., and Stevens, G. W.: Value of Routine Radiographic Examinations of the Newborn Based on a Study of 702 Consecutive Babies, Am. J. Obst. & Gynec. **20**:73 (July) 1930.

10. Epstein, I. M.: The Cause of Death and the Incidence of Disease in Children: A Review of One Thousand Consecutive Necropsies, Am. J. Dis. Child. **41**:1363 (June) 1931.

11. Hunt, C.: Cyanosis in the New-Born, Am. J. Dis. Child. **44**:1268 (Dec.) 1932.

12. Dunham, E. C.: Atelectasis in the New-Born, Am. J. Dis. Child. **43**:594 (March) 1932.

13. Henderson, Yandell: The Prevention and Treatment of Asphyxia in the New-Born, J. A. M. A. **90**:583 (Feb. 25) 1928; Incomplete Dilatation of the Lungs as a Factor in Neonatal Mortality, ibid. **96**:495 (Feb. 14) 1931; The Inhalational Method of Resuscitation from Asphyxia of the Newborn, Am. J. Obst. & Gynec. **21**:542, 1931.

tends to stimulate the sluggish respiratory center and causes adequate expansion of the lungs. Infants who breathe inadequately after birth are given this mixture of carbon dioxide and oxygen to stimulate deep breathing, in order that any atelectatic areas may become properly aerated and intervening pneumonia may be prevented.

Coryllos,[14] in this country, and Weimer,[15] abroad, have supported this method of treatment, which recently has come into extensive general use.

SUMMARY

A case of persistent congenital atelectasis is described in detail with complete roentgenographic and postmortem observations.

Cyanosis in new-born and young infants requires thorough clinical study and complete roentgenographic studies.

When cyanosis is due to atelectasis the infant should receive inhalations of a mixture of from 5 to 10 per cent carbon dioxide and oxygen.

6349 North Clark Street.

14. Coryllos, P. N.: Atelectasis, Asphyxia and Resuscitation in the Newborn, Am. J. Obst. & Gynec. **21**:512, 1931.

15. Weimer, R.: Treatment of Asphyxia in the Newborn by Means of the Carbon-Dioxide Gas Mixtures, Arch. f. Kinderh. **95**:65, 1931.

Progress in Pediatrics

OIL ASPIRATION PNEUMONIA (LIPOID PNEUMONIA)

CLINICAL, PATHOLOGIC AND EXPERIMENTAL CONSIDERATION

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ST. PAUL

Observation at necropsy of a peculiar pneumonia in infants which is believed to be a result of accidental aspiration of oily substances has been recorded infrequently. However, in the light of critical study of this condition as revealed in 7 necropsies of my own and of the data obtained on experimental animals, one is led to conclude that this is a distinctive pneumonia of relatively common occurrence, in which not only does the aspiration of oil play a dominant etiologic rôle but the clinical history and the pulmonary lesion are sufficiently constant and characteristic to merit its consideration as a clinicopathologic entity. The term "oil inspiration pneumonia" is suggested in preference to the "lipoid pneumonia" of the more recent authors.[1] It may be defined as an interstitial, proliferative pneumonia, usually localized, of low grade intensity, resulting primarily from the foreign body reaction of the pulmonary tissue to the presence of oil or fat, coupled, in most instances, with exudative inflammation due to the secondary invasion of bacteria and chemical irritants. The pneumonia is characterized by the conspicuous presence of oil-laden macrophages and giant cells which makes the diagnosis possible. It usually occurs in debilitated infants and runs a slowly progressive, chronic course, often with recurrent attacks of a low grade infection of the respiratory tract. As a rule, it subsides gradually and spontaneously with gain of health and resistance. In a few instances, however, it may develop into a chronic respiratory syndrome, diagnosed as chronic bronchitis, asthma, bronchosinusitis, etc. In a few other cases, acute septic pneumonia may complicate the primary process, and death may result from secondary pneumonia, from general sepsis or from a coexisting independent cause.

From the Pathological Service of the Children's Hospital, the Gillette State Hospital for Crippled Children and the Chas. T. Miller Hospital, St. Paul, and the Department of Pathology, University of Minnesota, Minneapolis.

1. (*a*) Rabinovitch, Jacob, and Lederer, Max: Lipoid Pneumonia, Arch. Path. **17**:160 (Feb.) 1934. (*b*) Holt, L. E., and Howland, J.: Lipoid Pneumonia, in Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton-Century Company, Inc., 1933, p. 464.

INCIDENCE

The incidence of oil aspiration pneumonia is obscure. Few cases are on record in which a clinical diagnosis of this condition was entertained with reasonable certainty. Innumerable cases, on the other hand, have undoubtedly failed of recognition at necropsy. It is highly probable that an appreciable proportion of the cases of "bronchopneumonia" in debilitated young infants diagnosed at necropsy may, on careful microscopic investigation, prove to be instances of primary oil aspiration pneumonia on which is superimposed acute septic pneumonia. In the 101 consecutive necropsies performed on children in this laboratory during the past three years, 7 cases of oil aspiration pneumonia were recognized on reexamination of the routine microscopic sections of the lungs. In none of these cases was oil aspiration pneumonia recognized until the sections were rechecked with this possibility especially in mind.

Laughlen [2] found 1 case in 300 consecutive necropsies performed in one year. Pinkerton [3] reported 6 cases in 290. Holt and Howland [1b] saw 23 patients with "lipoid pneumonia" in seven years, and 14 of these were infants under 2 years of age. Since 1925, 18 cases have been reported by four American authors, all but 1 of which occurred in children. Five of my cases were in infants less than 12 months old.

The occurrence of this type of pneumonia in adults is probably less frequent. Two cases in adults were reported in Germany during the past year.[4] Recently, I saw chronic pneumonia of this type at necropsy on a woman of 69.[5] However, the etiologic factors concerned in these cases in adults as well as in those in older children are often such that the cases may well be considered in a separate group, although the pulmonary lesion produced is essentially identical with that in infants. Attention may also be called to the occurrence of acute septic aspiration pneumonia in debilitated infants; in this condition many droplets of aspirated oil (milk fat) may be present in the exudate, and it should be differentiated from true oil aspiration pneumonia.

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2. Laughlen, G. H.: Studies on Pneumonia Following Naso-Pharyngeal Injection of Oil, Am. J. Path. **1**:407, 1925.

3. Pinkerton, Henry: Oils and Fats: Their Entrance into and Fate in the Lungs of Infants and Children, Am. J. Dis. Child. **33**:259 (Feb.) 1927.

4. (*a*) Fischer-Wasels, B.: Tödliche Lungenschrumpfung durch Gebrauch von Mentholol, Frankfurt. Ztschr. f. Path. **44**:412, 1933. (*b*) Bodmer, H., and Kallós, P.: Ueber schwere Lungenschädigungen (Lungenzirrhose) infolge Aspiration von Paraffinöl bei therapeutischer Anwendung, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **136**:40, 1933.

5. Necropsy Protocol, Department of Pathology, University of Minnesota, 1934.

ETIOLOGY AND CLINICAL COURSE

Oil aspiration pneumonia is rarely observed among healthy breast-fed infants. The victim is, as a rule, an artificially fed, poorly nourished infant, usually not more than 15 months of age. Cod liver oil is often administered as a routine measure, and liquid petrolatum is given to regulate the bowels. Forced feeding or feeding by tube is frequently observed. There is usually a history of repeated infection of the upper respiratory tract, with nasal discharge, coughing spells or asthmatic attacks and sometimes clinical signs and symptoms of low grade bronchopneumonia. Nasal instillation of an oil as a routine is frequently ordered. Anomalies of the oral or nasal orifices, such as cleft palate and harelip, may be encountered.

Physical examination may elicit a bilateral central consolidation which persists into the quiescent periods with little or no fever. The infant is slow in gaining weight. General lack of resistance is often manifested by recurrent attacks of impetigo.

Accidental aspiration of oils in these infants is understood to take place either following the instillation of nasal drops containing such vehicles as liquid petrolatum and olive oil or with the administration (usually forced) of cod liver oil, castor oil, liquid petrolatum, milk, etc. The physical struggle of the baby is probably the principal factor in such aspiration, although oil in small quantities has been found to glide easily down the back of the throat into the larynx without exciting reflexes or causing a voluntary or conscious act of swallowing.

As a rule, the infant recovers from each attack, and the general health gradually improves under proper management, although a residual pneumonic process may persist indefinitely.

In older children and adults, accidental aspiration of oils may occur under somewhat different circumstances. For example, cases have been reported following administration of liquid petrolatum to a child in diabetic stupor,[2] forced feeding of cod liver oil to an infant with laryngeal paralysis [1a] and daily self-instillation of liquid petrolatum into the larynx in the treatment of chronic laryngitis.[4b]

The roentgenogram of the chest in cases of this type of pneumonia is often illuminating. There is usually a bilateral irregular, dense and wide shadow along the pulmonary roots which extends into the perihilar zone and sometimes into the field beyond. In the field the shadow is sometimes soft, mottled or feathery and is often sharply demarcated from the uninvolved parenchyma. The picture may remain unchanged for an extended period, and the process is only slowly progressive, suggesting a chronic, low grade and productive lesion. The roentgenographic appearance of the pulmonary lesion is

often that of the "pulmonary root infection" or "broncho-sinusitis" of Wasson,[6] usually thought to be secondary to a chronic infection of the upper respiratory tract. Because of the persistence of the shadow, the lesion has been interpreted as possibly tuberculous. The denseness of the shadow, the location of the lesion and its tendency to become circumscribed and its slow progress make a fairly typical appearance. Superimposed acute pneumonia may tend to exaggerate the shadow and confuse the typical picture. With the aid of an accurate clinical history and of roentgenograms of the chest, the clinical diagnosis of oil aspiration pneumonia may be ventured.

PATHOLOGIC APPEARANCE OF THE LUNG

The macroscopic appearance of the lung in oil aspiration pneumonia resembles that in bronchopneumonia. Occasionally, an anatomic diagnosis of lobar, chronic interstitial or unresolved pneumonia has also been made. The area of maximum involvement is usually present along the pulmonary roots and the immediate adjacent parenchyma. The pleura over it may show yellowish mottling. The pneumonic area is lumpy on palpation and firm and rubbery in consistency. Areas of atelectasis and emphysema may be present along the periphery. The cut surface is mottled with small areas of consolidation, showing a white to orange-yellow discoloration, sharply demarcated from, or gradually merging into, the adjacent meaty or grayish parenchyma. The varied discolorations depend on the amount, kind and age of the oil, the extent of fibrosis, the associated infection and the degree of congestion and edema. The surface may be comparatively dry. Thin, cloudy, milky fluid may be expressed in small amounts. Droplets of pus may be obtained in the presence of purulent bronchitis or secondary bronchopneumonia. Associated acute exudative pneumonia may alter the gross appearance to such an extent that recognition of the primary lesion becomes difficult. Red, meaty areas of atelectasis and grayish patches of bronchopneumonia may involve other parts of the lungs. A diffuse, homogeneous involvement of a whole lung may occur. Such a lung is somewhat diffusely fibrous and rubbery in consistency and presents on section a smooth, grayish-yellow surface from which thin, milky fluid may be expressed (case 4).

The microscopic picture of oil aspiration pneumonia may vary according to the kind and amount of the oil aspirated, the stage of the primary process and the character and extent of the complicating secondary pneumonia. The cardinal histologic criteria, however, remain essentially constant.

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6. Wasson, W. W., and Waltz, H. D.: The Relationship of Sinus Disease to Chest Disease in Children, Radiology **22**:432 (April) 1934.

1. Terminal bronchi and bronchioles. A few oils are irritating to the lining epithelium and may stimulate it to active hyperplasia or cause its desquamation or necrosis. The lumen may contain cellular débris and exudate in which droplets of oil become entangled. The peribronchial stroma is congested and edematous and may show infiltration of inflammatory cells in varying numbers. Purulent bronchitis and bronchiolitis are often encountered.

2. Alveolar walls. The alveolar capillaries are engorged and the septums edematous. The septal and probably the epithelial cells become conspicuous by hypertrophy and evident proliferation. The alveolar lining may apparently become epithelized through the proliferation of the bronchiolar epithelium. Fibroblasts also make their appearance. The septums thus become greatly thickened, and there is consequent narrowing and frequent obliteration of the adjacent alveolar spaces. There is consequently distortion of the normal framework of the lungs.

3. Macrophages. Rapid appearance of mononuclear cells or macrophages is a distinctive feature of oil aspiration pneumonia and may possibly place the whole process primarily in the category of a foreign body reaction. The macrophages play the rôle of phagocytes and actually ingest certain oils, form giant cells and stimulate fibrosis. They often fill the alveolar spaces in a solid mass and also freely invade the stroma. Many of the macrophages appear swollen and foamy or vacuolated, owing to the presence within the cytoplasm of oil in the form of a single globule or fine droplets or in emulsion easily demonstrated by scarlet red. More than one kind of oil may become phagocytosed by the same macrophage. The primary function of these cells appears to be to phagocytose the foreign oil and dispose of it by transporting it into the regional lymphatic capillaries or possibly by intracellular digestion.

4. Polymorphonuclear leukocytes. Migration of neutrophils is usually inconspicuous. It occurs with the invasion of pathogenic microorganisms which are introduced with the oil from the upper respiratory tract. It may also be stimulated by the irritating effects of free fatty acid which is known to be present in excessive proportions in certain oils or to be liberated through too rapid hydrolysis.

5. Aspirated oil. Much of the oil is undoubtedly disposed of through expectoration. The remaining oil in cohesive masses of varying size may completely or partly obliterate the alveolar spaces. A part of the free oil is phagocytosed by the macrophages as a foreign body and disposed of through the lymphatic channels or by expectoration. Certain animal oils may be partly hydrolyzed and digested, or they may become phagocytosed and undergo intracellular digestion.

REPORT OF CASES

CASE 1.—A girl, aged 18 months, was admitted to the hospital for repair of cleft palate and harelip and died four months later, after the operation. The baby was extremely emaciated and rachitic. She had been fed condensed milk since birth. Impetigo with elevation of temperature developed from time to time. The patient was given 1 teaspoonful of cod liver oil three times a day. She choked easily during feeding and had repeated infections of the respiratory tract. An operation for the repair of the cleft palate and harelip was performed, and death occurred a few hours later, as though due to choking from aspiration.

Necropsy.—The body was poorly nourished and developed. The right lung weighed 80 Gm., and the left lung, 60 Gm. Crepitation was poorly preserved. The cut surfaces were congested and slightly edematous. The bronchial mucosa was swollen and reddened, and the lumens were filled with brownish, gelatinous, mucopurulent plugs. The trachea were also loosely occluded by a semisolid mass of mucus.

Microscopic examination of the lungs revealed diffuse edema, congestion and engorgement of the alveolar capillaries and areas of extravasation. There were infiltration of lymphocytes and mononuclears in small numbers and a slight proliferation of fibroblasts in the stroma. Many vacuolated macrophages and light, foamy masses of fine, delicate outlines were noted within many of the alveolar spaces. There was evidence of intense bronchitis and peribronchiolitis with hyperplasia of the lining epithelium.

The diagnosis was chronic proliferative, interstitial pneumonia, probably due to the aspiration of oil, and acute bronchitis and peribronchiolitis.

CASE 2.—A boy, aged 3 months, was admitted to the hospital with a diagnosis of malnutrition and indigestion and died of pneumonia one month later. Soon after birth diarrhea and bronchopneumonia developed, from which he apparently recovered. He was gaining in weight on feeding with a formula. Soon after his admission, however, there appeared a profuse nasal discharge, cough and signs of bronchopneumonia in the upper lobe of the right lung. A continuous inhalation of steam and compound tincture of benzoin and nasal instillation of liquid petrolatum every two hours were ordered. There was purulent discharge from both ears in the last few days of life. The abdomen became distended and the skin deeply icteric on the last day.

Necropsy.—The body was poorly developed and ill nourished. The skin was deeply jaundiced and showed several petechial spots over the abdominal wall. There was a purulent discharge from the nose. The right lung weighed 53 Gm. The pleural surfaces were covered with a thick, hemorrhagic, purulent exudate. Crepitation was poorly preserved. The cut surface showed a red and pinkish atelectatic parenchyma. There was a small grayish area of consolidation in the central portion of the upper lobe. The left lung weighed 58 Gm. An area of consolidation occurred at the hilus and extended along the upper border of the lower lobe. The cut surface of this area was grayish, homogeneous and rubbery in consistency. The parenchyma elsewhere was atelectatic. The pleural surface was covered with thick, purulent exudate.

Microscopic examination revealed that in the pneumonic areas many of the alveoli were solidly filled by a mass of macrophages and others by clumps of polymorphonuclears. The septums were thickened by congestion, edema, infiltration of various inflammatory cells and proliferation of fibroblasts. Giant cells were conspicuous. The epithelium of the terminal bronchi and bronchioles was actively

hyperplastic, and the lumens were filled with desquamated cells and débris and clumps of pus cells. There were also vast areas of necrosis, due apparently to massive aspiration of liquid material (fig. 1).

The diagnosis was chronic proliferative pneumonia, due probably to the aspiration of oil and acute septic aspiration pneumonia.

CASE 3.—A boy, aged 10 months, was admitted to the hospital and died of bronchopneumonia after a stay of eight months. At the time of birth, spasticity of the hands and arms was noted. Bottle feeding was instituted when the baby was 1 week old. When 2 weeks old, he became ill and had a severe convulsion and a temperature which reached 109 F. The mother then noticed the rigidity of the feet. The patient was given 4 drops of viosterol twice daily and 15 Gm. of calcium lactate. He was fed with a Breck feeder. Elevations of temperature were frequent. There was a tendency for impetiginous lesions of the skin to develop on the various parts of the body.

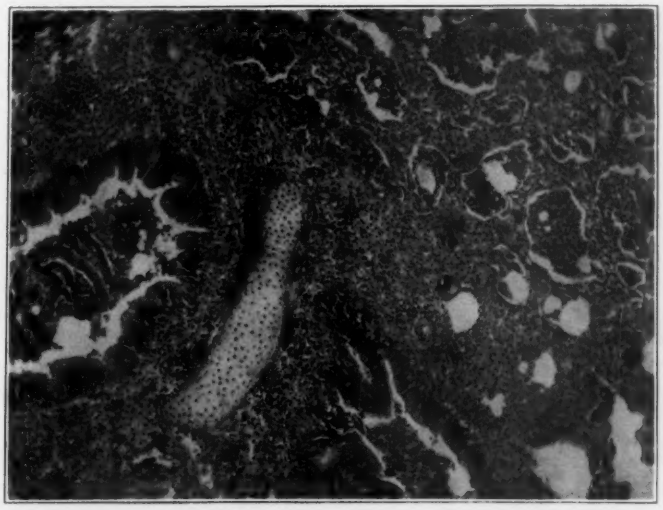

Fig. 1 (case 2).—Purulent bronchitis and peribronchitis with masses of macrophages within the alveoli, thickening of the alveolar walls and several giant cells scattered over the field.

The baby experienced difficulty in swallowing, which at times necessitated administration of drops of atropine sulphate (1:1,000) before feeding. He also had frequent regurgitations and attacks of cyanosis. At one time, there were numerous coarse râles in the chest, and the roentgenogram revealed the presence of bronchopneumonia. There was, at times, profuse nasal discharge, and an instillation of ephedrine and neo-silvol or ephedrine jelly was given. The patient was given liquid petrolatum regularly and later liquid petrolatum emulsified with agar.

Necropsy.—The body was well developed and fairly well nourished. The right lung weighed 90 Gm. Crepitation was reduced throughout. The pleural surfaces were covered with patches of thick, purulent exudate. The lower lobe on section appeared dark red and partially collapsed, and a few droplets of pus could be expressed. The left lung weighed 100 Gm. Its appearance was essentially the same as that of the right lung.

Microscopic examination revealed deep congestion of the alveolar and peribronchial capillaries as well as diffuse infiltration of lymphocytes, plasma cells and neutrophils, the latter appearing in clumps. Massive collections of macrophages were noted everywhere in many of the alveoli. Many macrophages were swollen and vacuolated and gave an orange-yellow reaction with scarlet red. These cells were distended with globules of oil, attaining three or four times the usual diameter and eventually rupturing to free the contents. The oil-laden cells migrated into the alveolar septums and were drained into the lymphatic capillaries of the alveolar septums, then into the perivascular lymphatic channels and those of the stroma. There were occasional giant and multinucleated cells containing globules of oil. There were conspicuous hypertrophy and hyperplasia of the cells lining many of the alveoli (epithelium?) and of the septal cells and a patchy increase in the cells of the connective tissue, which, with edema and congestion, produced thickening of the alveolar walls. There were inflammatory hyperplasia and desquamation of the bronchial and bronchiolar epithelium and a peribronchial zone of infiltrates. Many of the lumens were filled with purulent exudate or mononuclears and with cellular débris. The pleural surface was covered with a partly organized fibrinopurulent exudate.

The diagnosis was chronic oil aspiration pneumonia, purulent bronchitis and peribronchitis, suppurative pleuritis and bronchopneumonia.

Case 4.—A boy, aged 10 months, was admitted to the hospital with a diagnosis of double clubfoot and receding jaws which crowded the tongue into the throat. He died of pneumonia seven months after his admission. The baby was artificially fed from 1 month of age. He was given cod liver oil, 1 teaspoonful a day. A week prior to his admission, bronchitis and infection of the left ear and the tonsils developed. There was a slight cough. The baby regurgitated his feedings and vomited frequently, and it was necessary to feed him by means of a tube at times. Impetiginous lesions of the skin appeared from time to time; there was elevation of the temperature to as high as 107 F. A few days before death, the temperature rose to 108 F., and there was a corresponding elevation of the pulse and respiratory rates. There were showers of râles and bronchial breathing in the left lung and a few moist crackles in the right. A roentgenogram of the chest at this time showed patches of pneumonia in the lower field of the left lung and diffuse cloudiness of the corresponding field of the right lung with increasing density in the upper lobe.

Necropsy.—The body was poorly developed, poorly nourished and emaciated. The right lung weighed 72 Gm. The pleural surface was smooth and shining. Crepitation was diffusely impaired throughout. The entire lung was rubbery in consistency. The cut surface showed the parenchyma to be homogeneously orange-yellow, except along the periphery, and the bronchial walls to be thickened and prominent. A small amount of milky fluid was expressed, but no frank pus was present. The whole picture appeared to be due to diffuse fibrosis. The left lung weighed 50 Gm. Crepitation was well preserved in the upper lobe, but the lower lobe showed irregular consolidation. The cut surface was dark red, and a moderate amount of bloody fluid was expressed. A few droplets of pus were obtained from the bronchi.

Microscopic examination showed diffuse edema and congestion of the pulmonary parenchyma. Many of the alveoli were filled with a mass of foamy, vacuolated macrophages and giant cells which contained droplets and particles of oil (fig. 2). Large drops of free oil, taking a brighter stain with scarlet red, were noted in the distended alveoli and widened septal spaces. The intervening alveoli were obliterated by the proliferation of fibroblasts and septal cells and the

infiltration of macrophages as well as by masses of amorphous aspirated material (fig. 3). A few of the open alveoli were lined by a definite layer of what appeared to be epithelium. There were localized collections of neutrophils and lymphocytes.

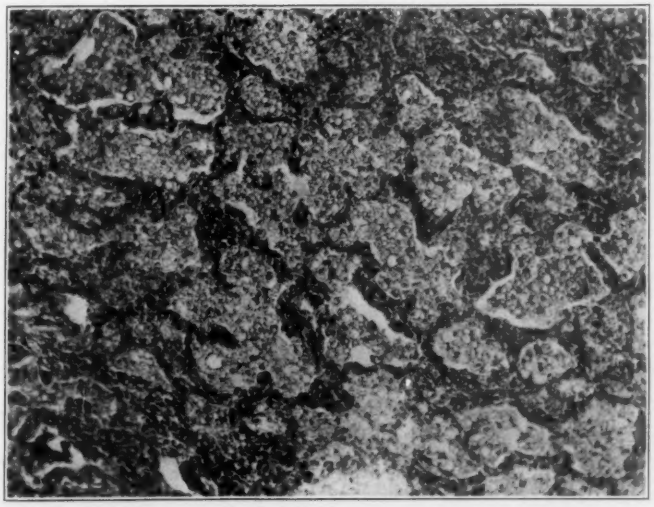

Fig. 2 (case 4).—Consolidation due in part to complete filling of the alveoli with solid masses of oil-laden macrophages (early stage of aspiration).

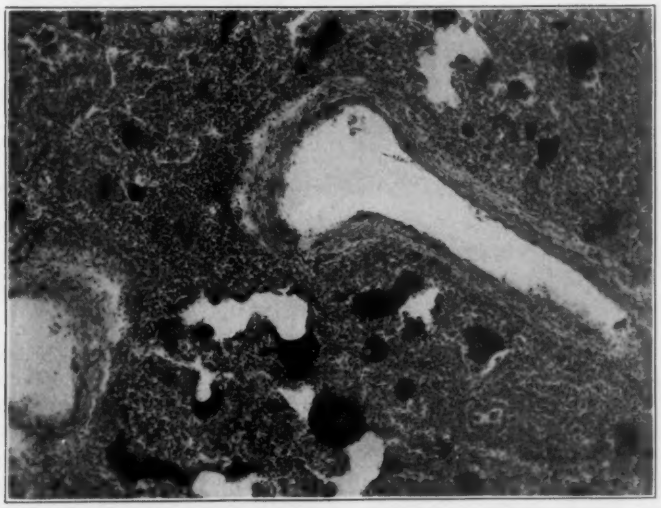

Fig. 3 (case 4).—Section from the upper lobe of the right lung (scarlet red stain), showing globules of oil in the dilated alveolar spaces surrounded by diffuse interstitial, proliferative inflammation.

The oil-laden macrophages showed a tendency to assemble in columns along the perivascular zones and in the interlobular connective tissue septums. The bronchioles were filled with desquamated epithelium and cellular débris.

The diagnosis was chronic oil aspiration pneumonia and acute septic aspiration pneumonia.

CASE 5.—A girl, aged 10 months, was admitted to the hospital because of spina bifida vera with meningocele and bilateral talipes equinovarus; she died of suppurative meningitis eight months after admission. The patient had been artificially fed since birth. The area presenting spina bifida soon became infected. There were frequent eruptions of impetigo. Instillations of drops of neo-silvol and ephedrine or of ephedrine jelly into the nose three times a day were ordered because of a nasal discharge. The baby was given cod liver oil. There were frequent regurgitations of the feedings. The patient died of septic meningitis and general sepsis.

Necropsy.—The body was poorly nourished and poorly developed. The right lung weighed 95 Gm. Crepitation was impaired throughout the parenchyma except

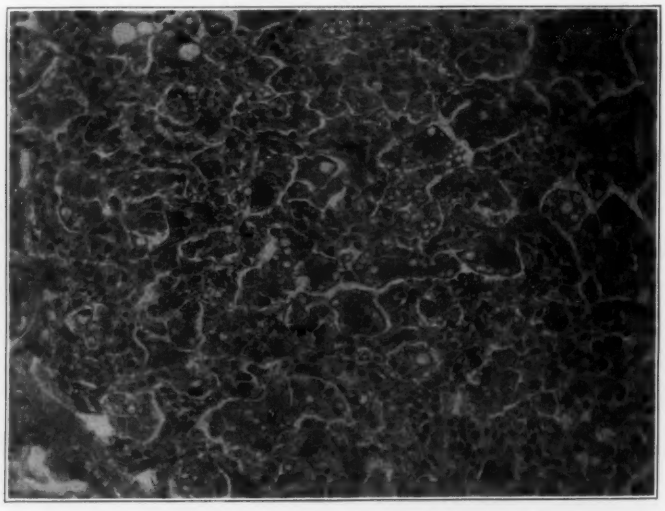

Fig. 4 (case 5).—View of an area of consolidation, showing many oil-laden macrophages and multinucleated giant cells which completely obliterate the alveolar spaces.

in the peripheral portions. In the solid portion, the pleura was stretched, shiny and dark red. On section the consolidated area was homogeneous and yellowish gray and showed distinct lobular markings. A small amount of thin, cloudy fluid was expressed. The left lung weighed 63 Gm. Crepitation was preserved throughout. The dependent portions were dark red and contained a slightly increased amount of fluid.

Microscopic Examination: The consolidation of the right lung was brought about by a massive collection of macrophages within the alveoli and by proliferation of connective tissue and septal cells (fig. 4). Vacuolated giant cells were many and conspicuous. Intense necrotizing bronchiolitis and accumulation of macrophages within the lumen were present. Many of the macrophages and giant cells were filled with oil droplets staining from orange-yellow to bright red (fig. 5). Free oil drops also gave reactions of similar shades. Columns of oil-

laden macrophages were noted along the bed of the peribronchial and perivascular connective tissue. Many of the open alveoli were lined by a layer of epithelial cells. There were small areas of necrosis, probably representing aspirated material.

The diagnosis was chronic oil aspiration pneumonia, purulent bronchitis and acute septic aspiration pneumonia.

CASE 6.—A girl, aged 3½ months, was admitted to the hospital because of difficulty in feeding and died of suppurative meningitis one month later. The baby was artificially fed from the third day of life. She caught cold and suffered from bronchitis, nasal discharge and snuffles. She was treated at home with nasal instillations of oil and inhalations of tincture of benzoin in steam. A part of each feeding was regurgitated, and the baby coughed considerably during the night when attempting to take feedings. She became cyanotic at times. Following her admission, nasal suction was applied from time to time, and drops of ephedrine

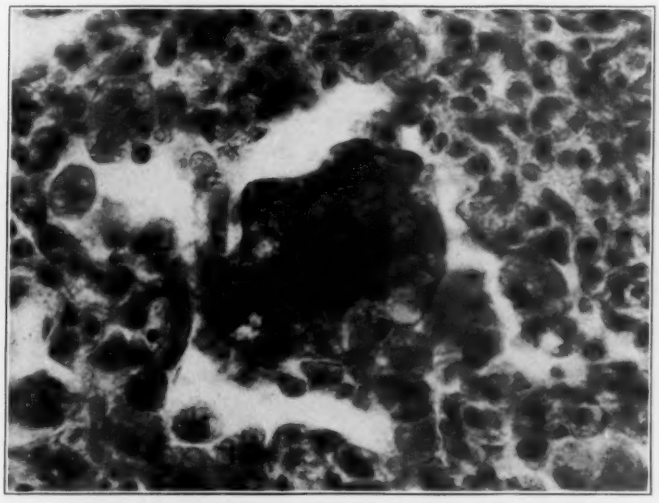

Fig. 5 (case 5).—A closer view of multinucleated giant cells ingesting globules of oil, some giving a bright red reaction and others lighter shades with scarlet red, indicating various stages of digestion, "age" differences of the same oil or more than one kind of oil phagocytosed by the same cell, or possibly all three of the processes. Proliferation of the septal and connective tissue cells as well as several oil-laden macrophages is seen.

and neo-silvol were instilled in the nose twice daily. Cod liver oil, one-fourth teaspoonful, gradually increased to 2 teaspoonfuls, twice a day, was ordered. A few days before death, the throat was acutely inflamed, and there were râles in the chest. The temperature rose to 108 F. A roentgenogram of the chest showed "marked bronchopneumonia of both lungs with relatively much less involvement of the lateral peripheral portions" (fig. 6).

Necropsy.—The body was poorly developed and poorly nourished. The right lung weighed 49 Gm. Crepitation was somewhat irregularly reduced throughout the lower portion. The cut surface was dark and mottled red, and the bronchial walls were thickened and prominent. There appeared to be areas of peribronchial

consolidation. There was an increased amount of bloody, frothy fluid. The left lung weighed 72 Gm. The pleura was thickened and fibrous in patches and covered with thick, membranous exudate. Crepitation was absent throughout. The whole lung was rubbery and fibrous in consistency. The cut surface showed prominent bronchial walls and small, patchy peribronchial areas of yellowish-gray discoloration. The intervening parenchyma was meaty, grayish and evidently diffusely fibrous. There was an increased amount of bloody, frothy fluid. No definite pus was expressed.

Microscopic examination revealed purulent bronchitis and bronchiolitis with massive collection of leukocytes in many of the lumens and in some of the alveoli. Alveolar exudate consisted of neutrophils and macrophages, the latter often predominating. Occasional giant cells were noted in the alveoli. There was a diffuse congestion of the alveolar capillaries with proliferation of the septal and connective

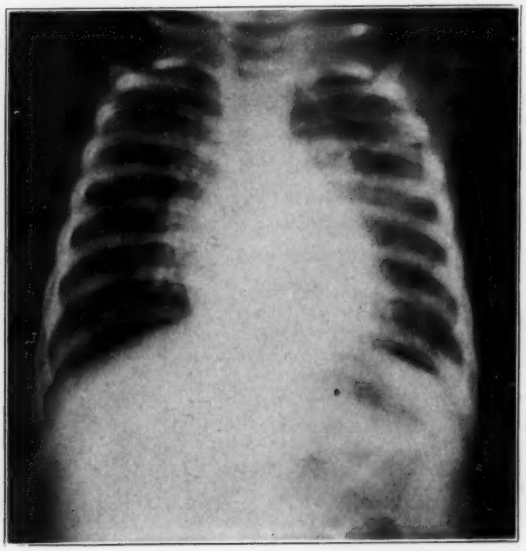

Fig. 6 (case 6).—Roentgenogram of the chest, illustrating typical bilateral perihilar consolidation, characteristic of oil aspiration pneumonia. There is extension into the upper fields.

tissue cells. Many of the macrophages were loaded with particles of oil, staining bright red, and there were a few free globules in the open alveolar spaces. The pleura showed marked fibrous thickening and organized vascular granulation tissue.

The diagnosis was oil aspiration pneumonia, purulent bronchitis and chronic suppurative pleuritis.

Case 7.—A girl, aged 21 months, was admitted to the hospital for repair of cleft palate and harelip and died a month later, immediately following the operation. Physical examination showed an undernourished infant. The baby had been bottle fed and had never taken her feedings well. She weighed 11½ pounds (5,216 Gm.). There was considerable nasal discharge. She was given 10 drops of halibut liver oil twice daily. At the completion of the operation she suddenly became cyanotic and died.

Necropsy.—The body was poorly developed and poorly nourished. The right lung weighed 40 Gm.; the left, 35 Gm. Crepitation was preserved throughout. There were small areas of brownish discoloration in the parenchyma of each lung with apparent partial atelectasis involving the portions along the bronchial tree. There were no areas of consolidation, and no pus was demonstrated.

Microscopic examination revealed, scattered about in the lung, many small, localized pneumonic patches, surrounded by a zone of emphysema (fig. 7). Conspicuous in the pneumonic areas were intra-alveolar masses of macrophages and giant cells, diffuse proliferation of connective tissue and septal cells and infiltration of a few neutrophils, eosinophils and lymphocytes. Drops of oil and macrophages filled with particles and globules of oil were demonstrated. Several of the larger masses of oil appeared thready and suggested beginning disintegration or digestion.

The diagnosis was chronic oil aspiration pneumonia.

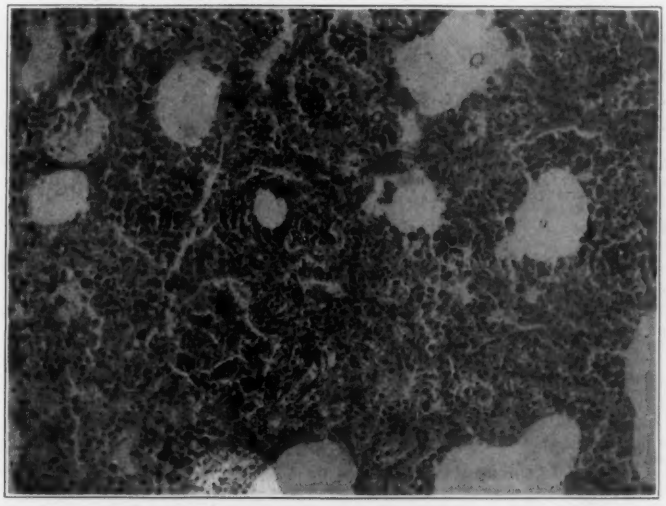

Fig. 7 (case 7).—Small miliary, nodular, proliferative pneumonic patches, showing a central mass of foreign body giant cells, some of which still retain a few minute oil droplets.

IDENTIFICATION OF OILS

Scarlet red, osmic acid and Ciaccio's stain were employed to identify the oil in the lungs in the last 4 cases. The identification of liquid petrolatum in the lungs in cases 4 and 5 was made through the negative reaction of the globules to osmic acid and Ciaccio's stain. Oils giving a positive reaction to osmic acid and the Ciaccio stain in the tissue in all 4 cases were assumed to be the oils recorded in the history as used in treatment. The oils gave the same shade of brownish black and light orange reaction to each stain. Many of the macrophages in the lungs in cases 4 and 5 contained oil globules which apparently reacted both positively and negatively to these two stains, possibly indicating the presence of liquid petrolatum and other oils in the same lesion. This

difference was also brought out by the different intensity in the color reaction to scarlet red of the oil globules within the same macrophage or giant cell. Disintegration or partial digestion of oil may also affect the staining in the same manner.

SUMMARY OF CASES

The following summarized data from the 7 cases are of pertinent interest (table). The ages of the patients in this series at the time of

Summary of Etiologic Data in Seven Cases of Oil Aspiration Pneumonia

Case	1	2	3	4	5	6	7	Summary
Age	18 mos.	3 mos.	10 mos.	10 mos.	10 mos.	3 mos.	22 mos.	Average 11 mos.
Sex	F	M	M	M	F	F	F	3 males: 4 females
Stay in hospital	4 mos.	1 mo.	8 mos.	7 mos.	8 mos.	1 mo.	1 mo.	5 mos.
Anomalies, etc.	Yes	None	Yes	Yes	Yes	None	Yes	5
Nutrition	Poor	Poor	Fair	Poor	Poor	Poor	Poor	6 poor; 1 fair
Period of breast feeding	None	None	1 wk.	4 wks.	None	3 days	None	3
Artificial feeding	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Impetigo	Yes	None	Yes	Yes	Yes	None	None	4
Regurgitation and vomiting	Yes		Yes	Yes	Yes	Yes		5
Nasal discharge		Yes	Yes		Yes	Yes	Yes	5
Previous respiratory infection	Yes	Yes	Yes	Yes		Yes	Yes	6
Use of cod liver oil	Yes		Yes*	Yes	Yes	Yes	Yes†	6
Use of liquid petrolatum‡			Yes					1
Use of oil given nasally		Yes	Yes		Yes	Yes		4
Probable oil producing pneumonia	Cod liver oil	Liquid petrolatum	Liquid petrolatum	Cod liver oil	Cod liver oil; liquid petrolatum	Cod liver oil; liquid petrolatum	Halibut liver oil	4 liquid petrolatum; 4 cod liver oil; 1 halibut liver oil

* Viosterol.
† Halibut liver oil.
‡ Administered by mouth.

death were 3 months, 3½ months, 10 months in 3 instances, 18 months and 22 months, with an average of less than 11 months. Five of the 7 patients were younger than 10 months of age. In each instance, a chronic ailment was evident, and the majority of the infants had a prolonged stay in the hospital. Breast feeding was denied from birth to 3 infants and was given for less than one week to 2 and for four weeks to 1. Artificial feeding was resorted to for all 7 infants. Nutrition was poor in 6 infants and fair in 1. Recurrent impetigo was present in 4 patients. Regurgitation of feeding was noted in 4 infants, while vomiting, choking or gagging with feeding was present in 3. Cod

liver oil was administered to 4 patients; halibut liver oil to 1 and liquid petrolatum as a laxative to 1. Oil was instilled nasally in 4 cases. A history of recurring respiratory infection was obtained in 6 cases, and at least 5 infants had purulent nasal discharge. Of the 7 patients, the two oldest had cleft palate and harelip; 1, spina bifida and hydrocephalus; 1, receding jaw and double clubfoot, and 1, cerebral spastic quadriplegia. Thus, 5 infants were suffering from either mechanical or neurogenic difficulties in deglutition. The cause of the death of 5 infants was terminal general sepsis with evidence at necropsy of bronchopneumonia or other atypical pulmonary infection, and in 2 older infants death was directly due to acute aspiration at operation. Purulent bronchitis was noted at necropsy in at least 5 of the 7 infants, while 4 showed histologic evidence of recent aspiration of feedings.

REVIEW OF CASES IN THE LITERATURE

In the 18 cases reported in the recent American literature, 4 by Laughlen,[2] 6 by Pinkerton,[3] 2 by Pearson [7] and 6 by Rabinovitch and Lederer,[1a] 1 patient was an adult of 37 and 3 were infants between 3 and 6 years, all of whom were suffering from serious illness which made aspiration of oil almost inevitable. The remaining 14 patients were infants less than 15 months old with the single exception of a child 30 months old. All of Laughlen's patients were given liquid petrolatum as nasal drops or as a laxative. The report of the series of Rabinovitch and Lederer gave meager information as to the manner of administration or the kind of oils given. Pinkerton and Pearson gave a fairly accurate account of the manner of administration of the various oils. Three of Pinkerton's 6 infants received liquid petrolatum by nasal instillation; 3, cod liver oil, and 2, liquid petrolatum as a laxative. Three received a combination of two oils, 2 receiving the oils orally and nasally and the third by mouth only. All of them had a previous history of repeated respiratory infection. Pearson's first patient received three oils, two orally and one nasally while his second received liquid petrolatum as a laxative. In most instances, the administration of these oils was for an extended period. All 18 patients showed at necropsy acute sepsis or bronchopneumonia which was the principal cause of death. In the majority of cases, sepsis played a dominant rôle, while many patients had a history of previous infection of the respiratory tract, often repeated. The pneumonic exudate was described as containing free droplets of macrophages laden with oil and fat which, in a few instances, predominated over the other cellular elements. Foreign body giant cells were sometimes conspicuous. In 4 of the patients evidence of fibrosis

7. Pearson, J. W.: Some Unusual Pneumonias Associated with the Aspiration of Fats and Oils in the Lungs, Am. J. Roentgenol. **26**:572 (April) 1932.

appeared in the alveolar septums and the stroma. In 2 older children, nodular areas of tumorlike fibrosis or granulomatous growth were observed.

REVIEW OF EXPERIMENTAL OBSERVATIONS

Although the intratracheal administration of preparations of antiseptic oils was practiced by Rosenberg [8] as early as 1885 and by Stewart,[9] Campbell [10] and others subsequently, reports on the histologic alterations in the lung following such administration are lacking. In 1917, experimental introduction of a mixture of iodoform and olive oil into the trachea was undertaken by Waters,[11] who saw a possibility of treating a pulmonary lesion and of simultaneously obtaining diagnostic roentgenograms of the lungs. They determined the lesion in the lungs of the animal thus treated to be that of a proliferative bronchopneumonia.

In 1920, Guieysse-Pellissier [12] studied the lungs of the animals subjected to the intratracheal injection of olive oil. His observation may be summarized as follows: The alveolar walls became considerably thickened around the masses of oil; the masses of oil appeared to be "eroded" at the edges and assumed a festooned appearance. This, he thought, was due to beginning lipolysis. At a more advanced stage of lipolysis, he noted a "lacelike" residue of fat. He expressed the belief that finally the fat was completely absorbed by the lipase. A part of the oil, however, was taken up by the cells—macrophages and eosinophils—which ingested it and probably produced intracellular digestion.

In 1922, Corper and Fried [13] reviewed the literature on the intratracheal injection of oils for diagnostic and therapeutic purposes and conducted experiments on animals, using chaulmoogra oil, olive oil and liquid petrolatum. The use of chaulmoogra oil in the local treatment of tuberculous laryngitis had just been reported by Lukens.[14] Corper

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8. Rosenberg, A.: Zur Behandlung der Kehlkopf- und Lungentuberculose, Berl. klin. Wchnschr. **24**:466, 1887.

9. Stewart, T. Grainger: On the Treatment of Bronchiectasis, Brit. M. J. **1**:1147, 1893.

10. Campbell, C.: The Treatment of Respiratory Affections by Means of Large Medicinal Injection Through the Larynx, Med.-Chir. Tr., London **78**:39, 1895.

11. Waters, C. A.; Bayne-Jones, S., and Rowntree, L. G.: Roentgenography of the Lungs, Arch. Int. Med. **19**:538 (April) 1917.

12. Guieysse-Pellissier, A.: Recherches sur l'absorption de l'huile dans le poumon, Compt. rend. Soc. de biol. **83**:809 (May 23) 1920.

13. Corper, H. J., and Fried, Harold: Intratracheal Injection of Oils for Therapeutic Purposes, J. A. M. A. **79**:1739 (Nov. 18) 1922.

14. Lukens, R. M.: Chaulmoogra Oil in the Treatment of Tuberculous Laryngitis, J. A. M. A. **78**:274 (Jan. 28) 1922.

and Fried observed that repeated intratracheal injections of chaulmoogra oil in amounts of 1 and 0.5 cc. in rabbits produced a condition varying from "a profound acute consolidation with abscess formation to a proliferative bronchopneumonia," death usually occurring in from two to ten days. They observed, on the other hand, only a mild type of proliferative bronchopneumonia after the injection of small amounts of olive oil and liquid petrolatum. They considered these two oils to be inert and to act only as a foreign insoluble substance.

In 1925, by oral as well as by intratracheal administration, Laughlen [2] was able to reproduce in rabbits the lesions he observed at necropsy in the lungs of the infants who received nasal instillations of menthol in oil and died of bronchopneumonia. He described an outpouring into the pneumonic areas of macrophages which phagocytosed the oil.

A comprehensive study of this subject was undertaken by Pinkerton, who reported, in 1927,[3] 6 clinical cases, with necropsy observations, of pneumonia associated with the aspiration of fats and oils and, in the following year, experimental data on the "Reaction of Oils and Fats in the Lung." [15] He reported the results of his study of the lungs of experimental animals following the intratracheal injection of various vegetable, animal and mineral oils. Through this investigation, Pinkerton contributed much to the present knowledge regarding the behavior of different oils introduced into the lung and the histologic appearance of the pulmonary lesions so produced in experimental animals.

On the whole, vegetable oils may be considered inert and harmless, and they show little microscopic evidence of hydrolysis or other chemical change. This is apparently due to the absence in the lung of a specific enzyme capable of hydrolyzing the oils. Owing to its high content of free fatty acids (28 per cent), chaulmoogra oil produces a severe degree of inflammatory reaction, while certain brands of olive oil of high fatty acid content (as high as 25 per cent) may act in a like manner. Animal oils tend to undergo hydrolysis in the lung by the action of a lipase preparatory to disposal. Fatty acids are thus liberated, often in excessive amounts as in cod liver oil, and stimulate inflammatory reaction, slow necrosis and fibrosis. Mineral oil causes no hydrolysis. It acts as a true foreign body and is rapidly taken up by the macrophages which pour into the alveoli and cause consolidation. The appearance of giant cells (which result from the coalescence of several oil-laden macrophages) and the production of fibrosis occur in a short time. Both animal and mineral oil are deposited in the regional lymph nodes, in which they may be demonstrated. Attempts were also made by Pinkerton to identify various oils through the application of differential stains for fat.

15. Pinkerton, Henry: The Reaction to Oils and Fats in the Lungs, Arch. Path. **5**:380 (March) 1928.

SUMMARY OF ANIMAL EXPERIMENTS

The results of my experimental work thus far obtained with rabbits subjected to intratracheal injection of such familiar oils as iodized poppy-seed oil 40 per cent, olive oil, castor oil, chaulmoogra oil, cod liver oil, halibut liver oil, cream, lard, rabbit fat, liquid petrolatum, ephedrine inhalant, metaphen and ephedrine, a mixture of menthol, oil of eucalyptus and liquid petrolatum, viosterol, etc., and killed or dying at varying intervals have been essentially identical with the observations recorded by Pinkerton. No detailed account of this work, therefore, is deemed necessary at this time. A few simple, fundamental observations of practical significance will be emphasized in the following paragraphs.

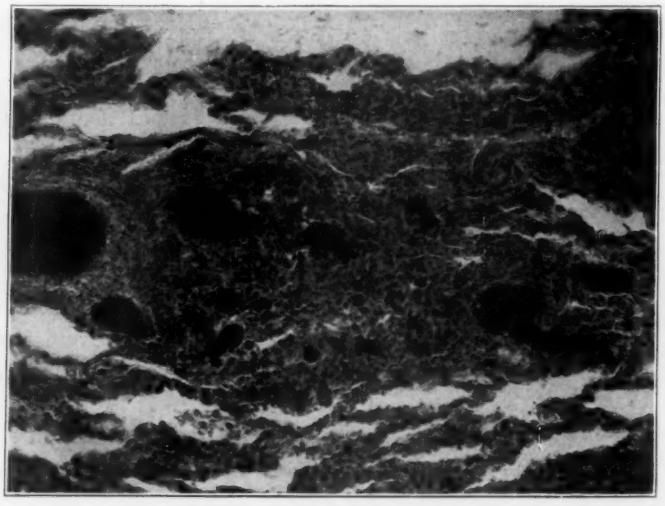

Fig. 8.—Localized nodular, proliferative pneumonitis about droplets of iodized poppy-seed oil, two and one-half weeks after the intratracheal injection of 3 cc. of iodized poppy-seed oil in a rabbit.

1. In all instances, the pulmonary lesions were produced by the intratracheal injection of oil with the animal under ether anesthesia. To demonstrate the possibility of ready aspiration of oil instilled into the nose, several rabbits were subjected to nasal instillation of a mixture of iodized poppy-seed oil 40 per cent and olive oil in amounts of 0.5 cc. daily for two or three days. Roentgenograms revealed the presence of the radio-opaque oil in the lungs of the animals so treated, strongly suggesting that the aspiration by babies of oil given nasally, when lying on their back, is in the realm of probability.

2. The immediate local effect on the lung of the aspirated oil is the production of localized hemorrhages and edema, owing to mechanical

obstruction of the alveoli by the oil. Should the amount of oil prove too large or the oil too irritating, death may result from massive hemorrhage and edema. The coincident introduction of pathogenic microorganisms and the high fatty acid content of certain oils may favor early exudative inflammation. Small areas of residual proliferative inflammation may persist.

3. All oils, including the relatively inert vegetable oils, such as iodized poppy-seed oil, may produce small areas of localized nodular, proliferative pneumonitis or interstitial pneumonia in rabbits in a few weeks (fig. 8). It is possible that a similar lesion may develop in man following intratracheal injection of iodized poppy-seed oil for diagnostic purposes.

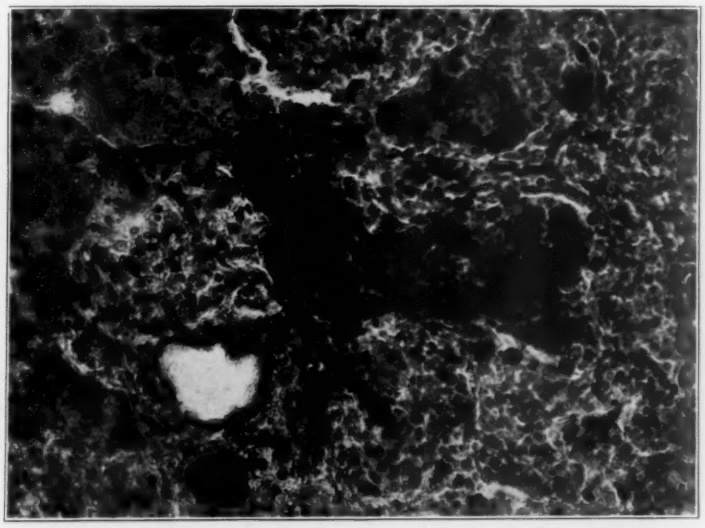

Fig. 9.—A large mass of oil in the lung of a rabbit, seen fourteen days after the intratracheal injection of cod liver oil, apparently undergoing digestion and thready disintegration.

4. Evidence of digestion or hydrolysis of animal oils is observed in experimental animals and also in man. This is shown by the irregular staining reaction and thready disintegration of masses of oil (fig. 9). Droplets and particles of oil so altered are also seen with macrophages.

5. Animal oils in general and other oils in combination with irritating drugs tend to stimulate the bronchiolar epithelium to marked proliferative activity which epithelizes the lining of the alveoli in immediate contact with the oil. This was strikingly demonstrated by cod liver oil and medicated mineral oils (figs. 10 and 11).

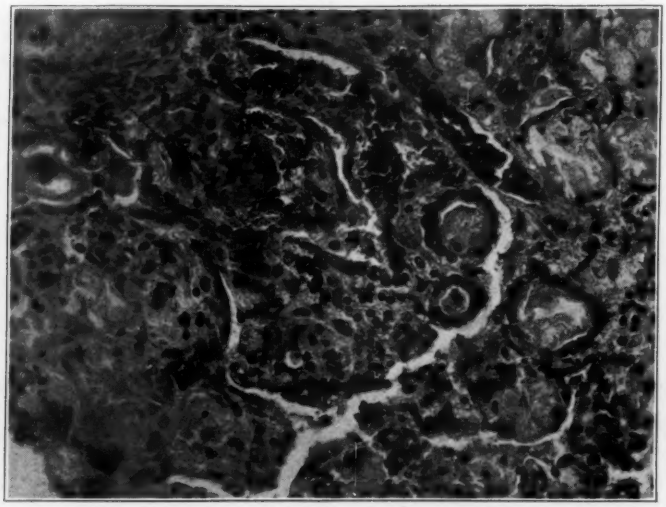

Fig. 10.—Masses of cod liver oil, seen fourteen days after intratracheal injection, within the alveoli of the lung of a rabbit, which are now lined by definite epithelium.

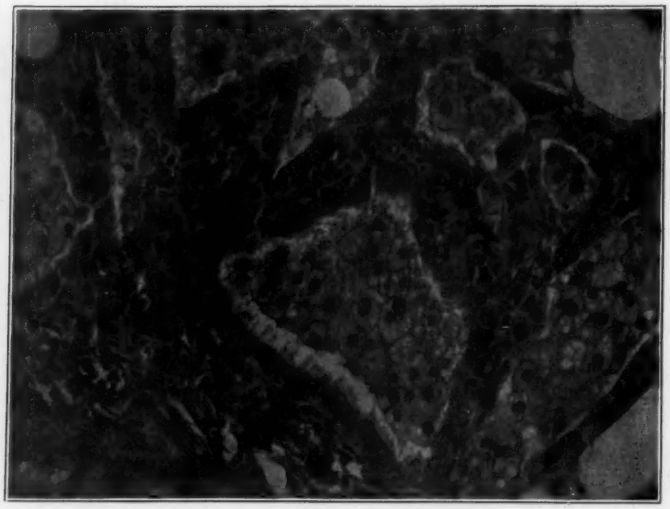

Fig. 11.—Epithelization of the alveolar lining fifty days after the intratracheal injection of 11 cc. of a mixture of menthol, oil of eucalyptus and liquid petrolatum. Oil-laden macrophages lie in masses within the alveolar spaces.

6. Owing to the high bacterial count, cream and milk may cause acute suppurative inflammation or abscess in the lung along with the proliferative lesion.

7. Oil-laden macrophages in large numbers migrate into the regional lymphatic chains for final elimination through the circulation.

8. Of the oils in general use, cod liver oil (or halibut liver oil) appears to be most damaging to the pulmonary tissue. It causes intense edema, congestion, fibrinous exudation, polymorphonuclear infiltration and active stimulation of the alveolar epithelium. A part of the oil may undergo oxidation and persist as a foreign body which stimulates the production of fibrosis and giant cells (fig. 12). Liquid petrolatum

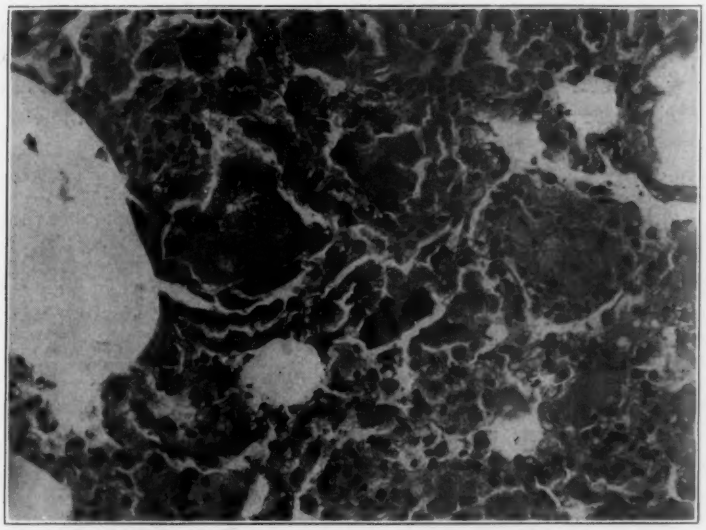

Fig. 12.—Fate of cod liver oil in the lung of a rabbit forty-five days after intratracheal injection. Solid masses of oxidized oil lie within the foreign body giant cells.

appears to stimulate foreign body reaction more readily than other oils. Alone, it causes no appreciable exudative inflammation. In combination with certain drugs it may induce proliferative activity of the epithelium as well as acute inflammatory reaction.

SUMMARY

Seven cases of oil aspiration pneumonia collected from a series of 101 consecutive necropsies performed on children are briefly reported and form the basis of the present study. The study embraces brief reference to the 20 cases already reported in the literature, including 3 occurring in adults, a short review of the experimental work by

several investigators on the effects on the lungs of various oils and fats introduced through the trachea and a brief summary of the results of similar experiments by myself. Cardinal diagnostic criteria are offered. The study may be summarized as follows:

1. The clinical syndrome and pathologic picture of pneumonia resulting from the aspiration of oily substances are observed to be fairly constant and characteristic.

2. Incidence of this condition is practically confined to the debilitated, artificially fed infant. Its frequency is appreciably greater than is generally known.

3. The fundamental pulmonary lesion, regardless of the kind of oil involved, is essentially a low grade, interstitial, proliferative type of inflammation, based primarily on the foreign body reaction toward the free oil of the tissues and variously modified by secondary complicating factors. The conspicuous presence of fat-laden macrophages and foreign body giant cells in varying numbers as well as the increase in septal connective tissue is the cardinal feature of oil aspiration pneumonia.

4. Only a limited number of oils and fats in use in treatment as a routine may actually become concerned in the production of the pneumonia. Liquid petrolatum and its various combinations, cod liver oil, halibut liver oil, milk and cream, castor oil and iodized poppy-seed oil may be mentioned. Of these, liquid petrolatum, cod liver oil (halibut liver oil) and certain medicated oils (usually with liquid petrolatum as the vehicle) appear to be by far the most important.

5. Pulmonary lesions comparable to oil aspiration pneumonia in man were easily reproduced in rabbits by the intratracheal injection of these oils.

CONCLUSIONS

Sufficient evidence has been put forth to justify the following general conclusions: (*a*) There is a possibility of causing local proliferative pneumonia of chronic tendency in infants through the accidental aspiration of oil administered through the mouth or into the nose; (*b*) such pneumonia, though relatively benign in itself, may often develop into one of serious clinical consequences; (*c*) therefore, more than passing caution should be employed when such administration is prescribed, particularly for debilitated infants, and, finally, (*d*) oil aspiration pneumonia should be considered as a distinct clinical and pathologic entity.

Pediatrics in Art

FRENCH DEVICES USED IN CHILDHOOD

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The accompanying illustration is a detail from a print entitled "Tableau de la vie humaine" which was engraved by Alexandre Jan, an eighteenth century artist, and is now in the Cabinet des Estampes in the Biliothèque Nationale, in Paris. It depicts children from birth to adolescence, showing the binder used for the infants and a binder and a

Various devices used for children in the seventeenth century in France.

baillotte which is still to be seen in use in Charente. The *baillotte* was often made of plaited straw or rushes and furnished a stiff support for the child, who when placed in it was stood about almost any place, which must have been most uncomfortable. The child was placed in this contrivance when it was 6 or 8 months of age, the binder on the legs enabling it to stand. The older infant in the illustration has a walker or "chariot," and the older child, a hobby-horse or "dada." The long clothes on the children at all ages are noticeable. A child who was able to walk was often put in a *virounou*, which allowed it to walk around in a circle. The *virounou* consisted of a pole so fixed that it would turn easily; the child grasped a horizontal bar and was suspended from the top of the *virounou* in a sort of sling, so that it could neither get out nor fall.

Pediatric Biographies

CARL LUDWIG VON ELSÄSSER
1808-1874

A NOTE ON THE HISTORY OF CRANIOTABES

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BALTIMORE

Carl Ludwig von Elsässer (1808-1874) was the son of a well known physician of Stuttgart, who described the occurrence of hemophilia in a family in Hufeland's *Journal der practischen Arzneykunde und Wundarzneykunst* in 1824. Carl von Elsässer is best known for his studies on cholera (Stuttgart, 1832) and for the theory of the manifestations of life in compressed air (Stuttgart, 1866). Hirsh did not mention von Elsässer's book on craniotabes, which is the first extensive—perhaps a bit too extensive—account of this condition. It is entitled: „Der Weiche Hinterkopf, Ein Beitrag zur Physiologie der ersten Kindheit. Mit Untersuchungen über die Entwicklung der Säuglingsschedels, überhaupt über die Rhachitis dieses Alters und über der Tetanus apnoicus periodicus infantum" (The Soft Posterior Head. A Contribution on the Physiology of the First Childhood with Investigation in the Development of the Infant Skull, Chiefly on the Rickets of this Age and on the Periodic Apnea of Infants). This work was published in Stuttgart and Tübingen by the J. G. Cotta'schen Verlagin in 1843. It is inscribed to his teacher and father-in-law, Dr. F. G. von Gmelin, who was professor of medicine in Tübingen.

It may be mentioned in passing that von Elsässer persuaded his brother, H. von Elsässer of Neuenstein, to use a child whom he had observed and whose body he had sectioned as the basis of his inaugural dissertation. This was entitled "Ueber eine widernatürliche Verdünning des Hinterkopfes bei einem Kinde," and was read under the auspices of Professor von Gmelin in the year 1837, at Tübingen. Carl von Elsässer named the condition craniotabes infantum.

Carl von Elässer's work consists of two hundred and fourteen pages and two plates and gives in detail the clinical histories of thirty-one cases of the more than forty which he had observed. It is a masterpiece of Teutonic thoroughness, starting with anatomic considerations and devoting some pages to pathology; the reports of cases follow some generalities, the apparent causes, the treatment and a short note on the

medicolegal aspects. Owing to the prolixity and to the repetitions of the essay it is difficult to quote from it, but the following excerpts are some of the high points.

His second case is given as follows:

The sixteen week old son of the landlord S. in Pfizhof, was put before me in March 1840. The father and mother were young, healthy and strong. The four other older children, all blooming had not suffered from this complaint. The child was nursed at the breast. Up to about 14 days before my visit it had been healthy but a trifle restless at night but still well nourished, blooming and had firm flesh but sparse hair on the head. I did not make a note on the large fontanelle. For 14 days it had a cough and frequent vomiting and with both of them there was much mucus. The sleep became more broken in which the head was moved to and fro and it slept most quietly on its side. It was easily frightened, often became suddenly pale without evident cause and sweat a great deal. The bowels were irregular, sometimes loose, sometimes constipated. Before I examined the head I said to the parents that the back of its head was too soft and to their surprise showed them that the lambdoidal suture was an inch broad and impressionable like stiff paper and like it could be indented, while the back of the head and the parietal bones had numerous large and small holes in them, which were clearly palpable. I merely recommended to accustom the child gradually to washings with cool water, including the head, and on account of the cold to take good care of it. A half year later, on a hurried trip through I found the child healthy.

GENERAL PICTURE

. . . The children who have craniotabes are for the most part born of weak individuals. To designate the inborn constitution more exactly, it involves a disposition to a slower development of the child. Such children are small, more or less thin, their flesh rather flaccid than elastic and hard, their skin rather pale than red. Their sutures remain movable and open longer; the posterior and lateral fontanelles are open some weeks or months, the anterior fontanelle is the same size as at birth; the edges of the bones, at least the ones bordering the fontanelles are with little force, impressionable. The children have sparse, short, fine hair. They commence later [than the average child] to laugh, to pay attention with eyes and ears, to play with others, to grasp and hold with the hands, to sit alone and to play by themselves. They get their teeth later, learn to stand and walk later. The anterior fontanelle decreases in size more slowly and takes longer to close. The thymus is larger and remains so longer. The children can however be entirely well and in the lesser grades of this constitution and favorable surroundings will by the second or third year be recovered of what was wanting and be equal to the more strongly born children.

In general, however, they have a greater inclination to illness and less resistance and adaptability to the vicissitudes of the world. A characteristic of this constitution is the greater softness of the bones (which must be differentiated from the disease). When after the passing of the first two to three months, the sense life of the child begins to expand, a shorter time is spent in sleep, then he begins to pay attention to his surroundings with eyes and ears and to wonder, then there is more active metabolism in the brain, a greater flow of fluid. The corresponding parts of the bony walls seem also to take part in this. The skull is in this period, more succulent, softer and on pressure inclined to give way before the turgid brain. So it may be explained that in children from the fourth month one finds

a thinness and impressionability of the posterior skull which in younger children is seldom seen. This is chiefly just in those children with the so called weak constitution that have soft bones beforehand.

Many of these children, namely the weaker ones, are from the beginning restless, and have disturbed sleep, cry frequently and seem to have pain although the cause is not clear. There are frequent bowel upsets which are manifested through colic, gas, constipation or diarrhea, the recognizable cause or accompaniment of the unrest. In addition these children are easily frightened and inclined to convulsive movements of the muscles of the face and eyes. Many sweat a great deal, and the skin shows a purple eruption. . . .

The symptoms of the dyscrasia must be described. To these belong the unusual sweating and partly too the broken sleep and movements of the head. Indeed the sweating as such disturbs the child and causes it to change its position frequently. It must also be remarked that the sweating in marked craniotabes is particularly profuse and partly on the back of the head. The sensitiveness of the head and the higher grades of night restlessness show clearly that the head lying particularly on its posterior part, causes the child discomfort and pain and the irritation of the brain causes sleeplessness. Furthermore the unusual apprehensiveness of the child and in many severe spasms belong here.

Generally the characteristic symptoms of our disease appear first in the third or fourth month. Either it appears in children previously well or with the above symptoms which are not uncommon in weak children. There is frequently some intercurrent acute affection as a chest catarrh.

The children become restless in sleep; if this existed it becomes worse. They wake every quarter to half hour whining or crying. Also in sleep but more on awakening and afterward they move the head on its long axis as if some unpleasant or painful thing was between the head and the pillow. They bore into the pillow, or raise up or bang the head over the pillow and move the arms over the head. When rocked, given a drink, having the head rubbed or lie on the side they go to sleep again. This broken sleep may be noted apart from evidence of pain. The children are restless, whine and cry without awakening. They always lie more quietly on the side than on the back. Many sleep with half open eyes, the eye ball turned and are often frightened in sleep. . . .

The nervous system is irritable, the child easily frightened and pulls itself together at every strong sense impression, as when someone approaches the cradle quickly or speaks loudly nearby. . . . The child also has a tendency to become pale often very quickly and without any apparent cause. [Then follows details of other rachitic changes.]

. . . There are spasms, tonic and clonic, which last from a second to half an hour. They come on daily once or more frequently and may continue daily or week long. In the pauses the child is relatively well. Frequently the child dies, after more or less frequent recoveries from the attacks. . . .

In tetanic convulsions the breathing is either stopped, the cramp reaching the organs of respiration or the breathing continues with more or less disturbance. . . .

It is a rule that nearly half of the craniotabetic children suffer from severe spasms in the third trimester. . . .

1. The thinned, perforated places are always on the back of the skull, or to describe it more exactly on the posterior bald half of the skull on that part of the same which on lying on the back lies below the level of its greatest, somewhat

median horizontal diameter. In front of or above this boundary one does not find such places.

2. On the inner surface of the skull there are hollows which correspond to the thinned, perforated places, impressions in the bone substance in which the convolutions of the brain lie. The raised ridges between the cavities correspond to the sulci separating the gyri on the surface of the brain. . . .

Often the thinning is found more on one side than the other. Here one finds on inquiry that the child preferred to be on that side which often depends on whether the bed of the mother or nurse, to which it turns its face, lies on the right or left side of the cradle.

Thus the thinning is always in the side of the skull under the brain. . . .

In most of the children with this disease, where corpses were opened showed an unusual softness of the rest of the skeleton. And apart from this showed deformities of the chest vertebrae, and long bones which was taken as an evidence of rickets. . . .

If one puts these two together, it cannot be denied that craniotabes belongs to that dyscrasia which has long been known under the name of rickets. . . . This shows itself especially in the nursing age in the suffering of the skull bones and the consecutive thinning of the posterior part of the skull. Craniotabes is the form of rickets of the nursling. . . .

Physicians, through ignorance of skull rickets, have concluded that rickets appear first after the first teeth are cut and that it does not affect the skull. . . .

I believe that the spasm attacks, which are found in half our cases, so often with a fatal outcome, are to be explained as having a casual relation of the accompanying disease of the skull, and have already noted one need not seek the cause otherwhere than in the nervous system. . . .

There remains only some special references on the tetanic-apneic attacks which we observed in most of our children. Between the tetanic attacks, with and without apnea, which we noted in half our cases of craniotabes, mostly in the second half of the nursing age, there appeared to be no essential difference but only one of degree and of extensive difference, only that in the first an irritation of the nervous system caused the proceeding convulsion to reach the respiratory apparatus and in the last it did not. . . . Our tetanic-apneic attacks are indistinguishable from what the writers call infantile asthma—thymic asthma—intermitting infantile dentition—periodic acute—spasmus glottidis, laryngismus stridulus, and *Juckkrampf* (laryngismus stridulus).

News and Comment

SOCIETY NEWS

New England Health Association.—The jubilee meeting of the New England Health Association will be held Friday, May 31, and Saturday, June 1, at the Massachusetts Institute of Technology. The program will be taken up largely with discussions on health education for children. For program reservations and further information apply to the secretary, Mrs. John Fuller, Massachusetts Institute of Technology, Cambridge, Mass.

Obituary

JOHN RUHRÄH, M.D.
1872–1935

Dr. John Ruhräh of Baltimore, a widely known and much beloved pediatrician, died at the Mercy Hospital, Baltimore, on March 10, 1935. He was born on Sept. 26, 1872, at Chillicothe, Ohio.

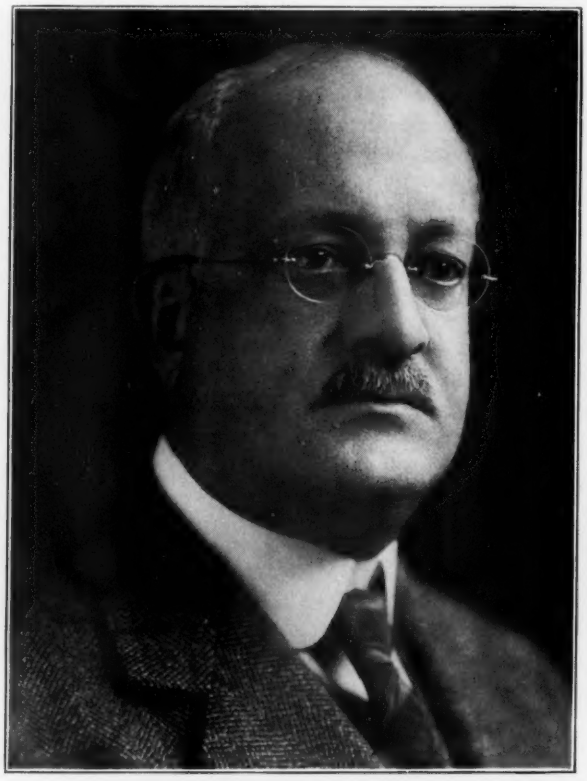
In October, 1930, after attending the International Pediatric Congress at Stockholm, he suffered an attack of poliomyelitis, from which, after a long illness, he recovered sufficiently to enable him to resume his practice and also to travel and to engage in many of his lifelong activities, though a residual paralysis of his lower extremities persisted. Early in January 1935, while examining a patient in his office, he was suddenly attacked with what appeared to be an apoplectic seizure. He was removed to the Mercy Hospital on January 17. His mind was clear almost to the last, and during his final illness he retained the fine humor and stoicism which had characterized his whole life.

Dr. Ruhräh graduated from the Chillicothe High School in 1891 and received his medical degree from the College of Physicians and Surgeons, Baltimore, in 1894. He took postgraduate courses at Johns Hopkins Hospital Medical School, at the Institut Pasteur in Paris in 1897 and at the universities and hospitals of Vienna, Berlin and Paris in 1900-1901. He was assistant resident physician at the Mercy Hospital in 1894-1895 and resident physician from 1895 to 1897. He was physician in charge of the Pasteur department of the College of Physicians and Surgeons in 1897. From 1898 to 1900 he was quarantine physician at the port of Baltimore. At about this time he was appointed to the chair of diseases of children at the University of Maryland Medical School, a position which he held for many years. He was also visiting physician to the Mercy Hospital, consulting physician to the Church Home and Infirmary and visiting physician to the Hospital for Women of Maryland. He never married.

He was elected president of the Medical and Chirurgical Faculty of Maryland in 1919, of the American Pediatric Society in 1925, of the Medical Library Association in 1927, of the Research Society in 1932, of the Osler Historical Society in 1933 and of the American Academy of Pediatrics in 1934. He was a member of the Board of Education of Baltimore. In 1932 he was selected by the Baltimore City Medical Society to prepare a history of the medical profession in Maryland for the last quarter of a century, a task which he was well qualified to perform. He entered private practice in Baltimore in 1901, though he

continued his academic connections, teaching bacteriology, pathology and clinical medicine in the College of Physicians and Surgeons.

He was a facile writer. His style was terse, with occasional shafts of fine humor, and his wide reading in many languages manifested itself in his numerous pertinent references from many fields of literature. Among his books may be mentioned: "Diet in Health and Disease" (with Julius Friedenwald), sixth edition, 1925; "Dietetics for Nurses" (also



JOHN RUHRÄH, M.D.
1872–1935

with Friedenwald), fifth edition, 1924; "Manual of Pediatrics of the Past," 1925; "Pediatric Biographies," 1932; "William Cadogan, His Essay on Gout," 1925, and "Poliomyelitis in All Its Aspects" (with E. E. Meyer), 1917. Dr. Ruhräh contributed articles on pediatric subjects to most of the modern American encyclopedias and systems of medicine, among which may be mentioned: Osler's "Modern Medicine," "Nelson Loose-Leaf Medicine," Tice's "Practice of Medicine" and Abt's "Pediatrics." Dr. Ruhräh made the first collective investigation

of actinomycosis in the United States (1899-1900), and he introduced the use of the soy bean in infant dietetics (1909).

One of his impelling interests was his love of books, which showed itself in his passion for the study of "the old worthies" in the pediatric literature. During the past several years he has been a regular contributor to the AMERICAN JOURNAL OF DISEASES OF CHILDREN on the subjects of pediatric biographies and pediatrics in art. His biographic sketches refer to interesting pediatric writers of the past, and his art sketches to reproductions of interesting illustrations of various phases of child health and hygiene. He sometimes was given to writing verse, and at medical meetings he would become inspired to write a few stanzas suggested by the themes under discussion, in which he would humorously reduce the highly involved scientific presentations to common sense interpretations. His poem on infant feeding became famous.

Dr. Ruhräh was a man of imposing appearance. He was tall and before his affliction, erect. He had a matchless personality and a great facility for establishing enduring friendships. He had a charm and graciousness of manner which led one to feel at home in his presence. He was extremely tolerant. He forgave shortcomings and appreciated even the minor virtues of his fellow men. He mingled well with all classes of people. The lowly and untutored did not repel him, and he met the intelligentsia gracefully and with wonderful poise. He was a brilliant conversationalist, scintillating and entertaining. He was always reminded of a choice tale from a rare book or a forgotten author. It was a great treat to enjoy his companionship during a leisure hour.

His artistic tastes were not confined only to art and literature. He was also a devotee of fine music. It was said of him in Baltimore that he scarcely ever missed a worth while musical event at the Lyric Theater. He made the annual pilgrimage to Bethlehem, Pa., for the Bach musical festival, of which he spoke to his friends as one of the most important events of his year. On his numerous trips to Europe he made it a point to visit one or more of the summer music festivals.

Dr. Ruhräh lived a full life. He combined the activities of the practitioner of medicine with a large degree of human understanding and common sense. He had an artistic nature and craved the cultural things in life. These he found it possible to provide for himself. After his severe affliction, by undaunted courage and indomitable will he was happily able to resume his work and his recreations. He gradually took on new tasks and carried on with joy and zest until the final illness. John Ruhräh leaves a rich heritage of devoted service, dedicated to medicine and to humanity.

A man beloved, a man elect of men.—Swinburne.

I. A. A.

Abstracts from Current Literature

Anatomy and Physiology

VITAL AND SUPRAVITAL STAINING OF ERYTHROCYTES. ALDEN B. DAWSON, Anat. Rec. **56**:143, 1933.

Nittis concluded that the granules and reticulation seen in erythrocytes stained vitally or supravitally were a new formation in the cell as a result of toxic damage and death of the cell.

Dawson daily injected intraperitoneally brilliant cresyl blue and neutral red into the adult necturus. He found that small doses of either had no effect. Intermediate doses brought the granules out, and large doses caused damage and death of cells, as evidenced by secondary formation of granules. The brilliant cresyl blue is more toxic, as there was phagocytosis of dead cells when this was used in large doses. Patterns of reticulation were not produced with sublethal doses of either dye.

SNELLING, Toronto, Canada.

ACCESSORY LOBES OF THE APEX OF THE LUNG IN INFANCY. PEDRO DE ELIZALDE, EUGENIO ZUCAL and JORGE PICCO, Prensa méd. argent. **21**:155 (Feb. 24) 1934.

The authors review the literature and discuss anatomically and pathologically the lobule of Wrisberg, which was first described in 1778. They found six instances in 2,000 children studied roentgenologically. Roentgenograms of the condition are shown.

SANFORD, Chicago.

STUDIES OF GROWTH BY MEANS OF HEPATOLIENOGRAPHY. ECKART BOTTERMANN, Monatschr. f. Kinderh. **59**:161, 1934.

The author attempted to determine the rate of growth of the liver and spleen in guinea-pigs by means of roentgenograms taken after the intravenous injection of thorium dioxide. The article contains eleven diagrams and photographs. Apparently, the growth of the spleen is irregular, varying greatly in different animals, and in some of the pictures this organ seems smaller than in preceding pictures. The liver's growth is not constant, but is more related to the age of the animal than is that of the spleen.

The author concludes that the methods employed are not sufficiently accurate as yet to determine the growth of the spleen, though they suffice to measure that of the liver. He concludes with the recommendation to other observers that the experiment be repeated with two injections and that the roentgenograms be taken at frequent intervals.

GERSTLEY, Chicago.

Pathology, Bacteriology and Biochemistry

STUDIES ON INFLAMMATION: X. THE CYTOLOGICAL PICTURE OF AN INFLAMMATORY EXUDATE IN RELATION TO ITS HYDROGEN ION CONCENTRATION. VALY MENKIN, Am. J. Path. **10**:193 (March) 1934.

It is suggested that the determination of differential leukocytes in an area of inflammation is a function of the hydrogen ion concentration of the exudate. When the exudate is alkaline, the polymorphonuclears are in excess; when it is neutral, the numbers of polymorphonuclears and mononuclears approach each other, and when it is acid there are many degenerated polymorphonuclears, with an excess of mononuclears. The changes in the hydrogen ion concentration may precede the cytologic changes.

MOORE, New York.

THE CULTIVATION OF MEXICAN AND EUROPEAN TYPHUS RICKETTSIAE IN THE CHORIO-ALLANTOIC MEMBRANE OF THE CHICK EMBRYO. S. ZIA, Am. J. Path. **10**:211 (March) 1934.

It was possible to infect the chorio-allantoic membrane of the chick with the Mexican and European types of rickettsiae of typhus fever, but it is improbable that this method could be used for the production of vaccine. The two varieties are morphologically identical, but reinoculation into guinea-pigs produces the two characteristic types of the disease.

MOORE, New York.

A CASE OF HODGKIN'S DISEASE IN A DOG. H. E. MACMAHON, Am. J. Path. **10**:309 (March) 1934.

A case of Hodgkin's disease in a dog is reported. No reports of similar cases could be found in the literature. The cervical lymph nodes were involved.

MOORE, New York.

THE EFFECT OF A DEFICIENCY OF VITAMIN B UPON THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM OF THE RAT. C. O. PRICKETT, Am. J. Physiol. **107**:459 (Feb.) 1934.

The data indicate that the site of the lesion responsible for the symptoms associated with a lack of vitamin B in the rat is in the central rather than the peripheral nervous system.

NOURSE, Cleveland.

THE EFFECT OF EXTRACTS OF THE ADRENAL CORTEX ON GROWTH AND REPRODUCTIVE SYSTEM OF NORMAL RATS, WITH PARTICULAR REFERENCE TO INTERSEXUALITY. EVELYN HOWARD and ARTHUR GROLLMAN, Am. J. Physiol. **107**: 480 (Feb.) 1934.

Cortical extract was injected intraperitoneally into growing rats in amounts equal to from two to seventeen times the normal physiologic requirement. No appreciable influence was noted on the size of the gonads, the estrous cycle, or the course of gestation. Sections of the pituitary gland, thyroid, suprarenals, ovaries and testes revealed no histologic abnormalities.

These results are of particular interest in connection with the clinical association of hypertrophic suprarenals and suprarenal tumors and virilism in the female, pubertas praecox or pseudohermaphroditism. Howard and Grollman state that their results do not support such opinions. They believe that the frequent but not invariable coincidence of intersexuality or precocious sexual maturity with suprarenal cortical tumor is probably a result of a common inducing factor.

NOURSE, Cleveland.

ROENTGENOGRAPHIC STUDIES OF THE ESOPHAGUS OF THE INFANT. M. LELONG and P. AIMÉ, Nourrisson **22**:1 (Jan.) 1934.

These studies were made on a series of seventy infants aged from 10 days to 18 months. The normal esophagus of the infant is large and ballooned out, resembling the mega-esophagus of the adult. Not infrequently there is a slight to moderate narrowing at the level of the aortic arch.

As soon as any substance gains entrance to the esophagus from the pharynx it is passed along to the cardia by energetic peristaltic waves. The cardia offers but little resistance at the lower end of the esophagus. The esophagus of the infant is assentially a compartment of the stomach.

The ballooning of the esophagus and stomach with swallowed air is much more likely to take place with liquid food than with solid feedings. Air is less likely to be swallowed when the infant is in the recumbent position.

MCCLELLAND, Cleveland.

PHYSIOLOGIC EFFECTS OF HIGH ALTITUDES. K. M. BUIKOV and E. E. MARTINSON, Ark. biol. nauk **33**:147, 1933.

This is a report of the results of several years' investigation of the physiologic effects of high altitudes in the Caucasian mineral water resorts (from 600 to

2,100 meters) on dogs and on man. In general, the previous findings of Barcroft and others are corroborated in regard to gaseous exchange, pulmonary ventilation, displacement of the hemoglobin dissociation curve and increase in the red blood cells and the effect of work on these factors. Study of the acid-base equilibrium showed that the hyperventilation leads to a decreased carbon dioxide tension and alkali reserve in the blood. This in turn leads to a shift of chlorides from tissues to the blood and from the blood cells into the plasma and to an increased excretion of chlorides in the urine. The excretion of inorganic bases is increased, but not as much as that of chlorides, which explains the increased titratable acidity of the urine. There is no increase in the excretion of organic acids. No evidence was found of an increased rate of oxidation of amino-acids or of tissue proteins, as evidenced by the concentration of amino-nitrogen and amino-phosphorus of the blood.

KUGELMASS, New York.

GASEOUS METABOLISM DURING MUSCULAR WORK: III. CHANGES OF OXYGEN SATURATION OF VENOUS BLOOD DURING THE PERIOD OF RESTITUTION. I. L. KAHN and M. K. MILOVIDOVA, Russk. j. physiol. **16**:155, 1933.

During the period of recovery from intense muscular work the oxygen capacity of the venous blood gradually falls to the level during resting, but the degree of oxygen saturation first rises, reaches a maximum within three minutes and finally falls, the maximum value corresponding with the minimum value of the coefficient of oxygen uptake.

KUGELMASS, New York.

NEPHELOMETRIC EXAMINATION OF THE SERUM. G. A. RADEMAKER, Maandschr. v. kindergeneesk. **3**:53 (Nov.) 1933.

The author is of the opinion that the nephelometric method of investigation of the serum proteins is reliable and deserves general application. He gives his results obtained with this method in a large number of clinical cases. Its prognostic value in tuberculosis is discussed.

VAN CREVELD, Amsterdam, The Netherlands.

MODERN OPINIONS ON THE PHARMACOLOGY OF IRON. S. E. DE JONGH, Maandschr. v. kindergeneesk. **3**:251 (March) 1934.

The author summarizes the findings of last year as follows: The empirical preference for iron was accounted for, and the rôle of ferrous compounds and ferric compounds was studied. The ferrous compounds were stabilized (Starkenstein). The investigations on the therapeutic value of copper compounds are discussed.

VAN CREVELD, Amsterdam, The Netherlands.

Nutrition

THE EFFECT OF ADDING LIVER TO THE DIET UPON THE GROWTH AND REPRODUCTION OF RATS. ALICE M. BAHRS, Am. J. Physiol. **105**:262 (Aug.) 1933.

Raw or cooked liver added to adequate stock diets and various milk mixtures caused increased growth of young rats. There was an apparent improvement in lactation when liver was added to the diet, as the number of young reared by the rats was greater and the young were heavier at 30 days of age than the young of animals which did not receive liver.

NOURSE, Cleveland.

STUDIES IN RACIAL METABOLISM: BASAL METABOLISM OF THE ARAUCANIAN MAPUCHES. J. PI-SUÑER, Am. J. Physiol. **105**:383 (Aug.) 1933.

The following observations on basal metabolism were made on Mapuche Indians of southern Chile. The basal metabolic rates of thirty-one men and fourteen women were determined with the closed circuit type of apparatus (Benedict-Roth

and Popular Krogh). The average values were 9.8 per cent above the Harris-Benedict standards for men and 14.8 per cent above those for women. Associated with the high values of basal metabolism was a pulse rate slower than normal for the white race—60 in men and 67 in women. These observations are similar to those on the Mayas of Yucatan, the only other aboriginal American race studied, and are different from those made on nonaboriginal American races.

NOURSE, Cleveland.

EFFECT OF DIET ON RESPONSE TO PARATHYROID EXTRACT AND VITAMIN D: I. THE RELATION OF CALCIUM AND PHOSPHORUS OF THE DIET TO RESPONSE TO PARATHYROID EXTRACT IN RATS. AGNES FRY MORGAN and JEAN G. FIELD, Am. J. Physiol. **105**:585 (Sept.) 1933.

Parathyroid extract in moderate doses produces a rise in serum calcium only when a good supply of calcium is available from the diet or from an accumulated reserve, probably in the bone trabeculae.

NOURSE, Cleveland.

EFFECT OF DIET ON RESPONSE TO PARATHYROID EXTRACT AND VITAMIN D: II. THE EFFECT OF HIGH CALCIUM-LOW PHOSPHORUS DIETS IN DOGS. AGNES FRY MORGAN and E. ALTA GARRISON, Am. J. Physiol. **105**:596 (Sept.) 1933.

Marked hypercalcemia resulted in dogs fed a diet high in calcium and low in phosphorus following moderate doses of parathyroid extract when vitamin D was included in the diet; little change was noted when vitamin D was omitted from the diet. Some evidence of healing of rickets was noted following injections of parathyroid extract in the animals fed a vitamin D-free diet.

NOURSE, Cleveland.

THE RELATION OF VITAMIN B REQUIREMENT TO METABOLISM. WALTER A. HENDRICKS, Am. J. Physiol. **105**:678 (Sept.) 1933.

In an attempt to estimate the maintenance requirements of growing chickens some results were obtained which suggest that the metabolism of an animal is proportional to the 5/3 power of the live weight.

Since Cowgill, in a recently published work (1932), showed that the vitamin B requirement of an animal is proportional to the 5/3 power of the live weight, it is probable that the vitamin B requirement is proportional to the metabolism.

NOURSE, Cleveland.

STUDIES IN THE NUTRITIONAL ANEMIA OF THE RAT. HOWARD H. BEARD and VICTOR C. MYERS, Am. J. Physiol. **106**:449 (Nov.) 1933.

Anemia was observed to develop during pregnancy in the rat. The reduction in hemoglobin averaged in excess of 20 per cent and exceeded 40 per cent in about one third of the pregnant animals. The reduction in red cells averaged about 40 per cent. The addition of iron to the diet of the pregnant rat appeared to exert some retarding influence on the fall in hemoglobin. Liver extract and yeast did not prevent the occurrence of anemia or hasten recovery after birth of the young.

NOURSE, Cleveland.

NUTRITIONAL STUDIES OF FOOD STUFFS USED IN THE PUERTO RICAN DIETARY: IV. EXTRACT OF THE ANNATTO SEED, BIXA ORELLANA; ITS PREPARATION AND PHYSIOLOGICAL PROPERTIES. T. H. COOK and J. H. AXEMAYER, Am. J. Trop. Med. **14**:61 (Jan.) 1934.

The authors give a brief history of the use of the seed of the plant Bixa orellana by civilized man. They also describe their technic for preparing alcoholic, chloroform and petroleum-ether extracts of the Bixa orellana seed. Numerous experiments were carried out with these extracts to determine their vitamin A

content. Experiments were also carried out to determine the vitamin A content of lard in which the seed had been extracted at the boiling point, and also the presence of vitamin D in lard extracts that were subjected to the sun's rays. The alcoholic, chloroform and petroleum-ether extracts were all found to contain a substance that functioned like vitamin A in the animal body, but the petroleum-ether extract contained the largest amount of it. The lard extracts were also found to contain large amounts of vitamin A; these contained in addition some vitamin D, but the exact amount was not determined. BURPEE, Augusta, Ga.

A SUMMARY OF VARIOUS TYPES OF INFANTS FED ON DRY MILK EXTENDING OVER A PERIOD OF FOURTEEN YEARS. MATHER M. MCCORD, Arch. Pediat. **50**:873 (Dec.) 1933.

The writer gives in a general way his impressions of the use of dry milk as a food for infants. WADDELL JR., University, Va.

GLUCOSE TOLERANCE STUDIES IN CHILDREN AND IN ADOLESCENTS. H. J. JOHN, Endocrinology **18**:75 (Jan.-Feb.) 1934.

In comparing glucose tolerance tests in 192 children with those in 1,500 adults, the following results were obtained: 1. Normal curves were secured in 82 per cent of the children and in only 62 per cent of the adults tested. 2. The normal blood sugar level during fasting was the same in children and in young adults, namely, from 60 to 120 mg. per hundred cubic centimeters, although most levels fell between 71 and 110 mg. 3. There was evidence that infections produce temporarily decreased glucose tolerance and may play a definite part in the production of permanent diabetes. 4. Of 52 children with glycosuria, 33 per cent showed a diabetic type of glucose tolerance curve, which is approximately the same percentage as was found in adults. 5. Of 14 obese children, only 2 showed decreased sugar tolerance, as compared with 65 per cent of obese adults.

JACOBSEN, Buffalo.

SOME ENDOCRINE OBSERVATIONS ON ADVANCED OSSIFICATION IN CHILDREN. W. A. REILLY, Endocrinology **18**:117 (Jan.-Feb.) 1934.

While retarded aging of bone is a common occurrence and is generally considered as an indication of hypothyroidism, accelerated aging of bone is rarely recorded. This report concerns twenty-two girls under observation in a clinic for diseases of the ductless glands because of obesity. All showed definitely advanced development of the epiphyseal center, with a tendency to premature development of secondary sexual characteristics and increased height. Seventeen had an early onset of menses, the average age for the group being 11 years and 2 months, as compared with a normal average age of menarche of approximately 14 years.

The obesity and overgrowth in height preceded the premature appearance of menses often by many years. The distribution of excess fat in the axillae and on the girdle and thighs and the pudgy hands resembled the condition seen in hypopituitarism. No similar syndrome in boys attending the clinic was noted.

It is suggested that these cases may be instances of primary preadolescent pituitary eosinophilism and basophilism, with secondary ovarian hypofunction, although the reverse condition is possible. JACOBSEN, Buffalo.

ADVANTAGES OF STRAINED SOLIDS IN THE EARLY MONTHS OF INFANCY. MANUEL M. GLAZIER, J. Pediat. **3**:883 (Dec.) 1933.

Two hundred and thirty-one infants in a clinic for well babies in Boston, varying in age from 2 to 10 months, were first fed strained solid foods, such as cereal, toast, egg yolk, fruits and vegetables. The infants were allowed to eat as much of the solid foods as they desired and were then offered the breast or

bottle. Those given solid foods during the second or third month showed a better gain in weight, earlier dentition, earlier walking, less constipation, better food habits and fewer dislikes for food than those who did not receive solid foods till later. The infants showed definite ability to digest strained cereals, vegetables and fruits during the second and third month of life, as was shown by inspection of the stools. The author believes that the giving of solid foods early in infancy produces better nutrition and habits, because there is an adequate amount of iron, vitamins and bulk in the diet and because the psychologic effect is beneficial.

LEMASTER, Evanston, Ill.

ON RICKETS. E. GORTER, J. Pediat. **4**:1 (Jan.) 1934.

When a mercury vapor lamp with a uviol glass bulb was used, 0.1 calorie of a wavelength of 2,970 angström units was the daily dose required to cure rickets in children. It was found that when an ergosterol preparation containing 10 per cent vitamin D was used, 0.02 mg. was usually insufficient, whereas 0.05 mg. was almost always effective in curing rickets. The use of an ivory wedge in determining the roentgen-absorbing material in bone is discussed.

LEMASTER, Evanston, Ill.

THE LIMITATIONS OF CEREAL-MILK DIETS FOR HEMOGLOBIN FORMATION. C. A. ELVEHJEM, E. B. HART and W. C. SHERMAN, J. Pediat. **4**:65 (Jan.) 1934.

The hemoglobin content of anemic rats was determined while they were on a milk diet supplemented by the following commercially prepared cereals: Ralston wheat cereal, Quaker Rolled Oats, Cream of Wheat, Mead's cereal and Wheaties. Cream of Wheat caused no rise in hemoglobin. The other cereals caused a moderate rise, but this was far inferior to that produced when inorganic iron, copper and manganese were added to the milk. The addition of copper alone to the milk-cereal diets caused a more rapid regeneration of hemoglobin at first, but eventually the hemoglobin level was about the same as with the milk-cereal diet. The addition of iron as ferric chloride to the milk-cereal diets caused rapid rise of hemoglobin to a high level. The addition of iron and copper produced better appearing animals, although the hemoglobin was not higher than when iron alone was added. The iron in Mead's cereal was slightly less available than that in Rolled Oats and Wheaties. In none of the cereals was the iron as available for hemoglobin formation as that furnished by ferric chloride. In view of these facts, it is suggested that the milk-cereal diets of children be constantly reinforced with foods rich in available iron or with iron salts standardized as to their copper content.

LEMASTER, Evanston, Ill.

GROWTH AND DEVELOPMENT. C. ANDERSON ALDRICH, J. Pediat. **4**:120 (Jan.) 1934.

The effect of vitamins on growth is discussed. Each vitamin is considered separately with reference to the pathologic changes resulting from vitamin deficiency and its effect on growth and development. The author attempts to answer the question: What attitudes should the pediatrician take toward the sellers of commercial vitamin products, the biochemists, the skeptics and the mothers of the patients? A lengthy bibliography is added.

LEMASTER, Evanston, Ill.

TWO SERIES OF CASES OF FOOD POISONING. LAWRENCE HENRY COTTER, New York State J. Med. **33**:698 (June 1) 1933.

Four children, aged 4, 5, 8 and 12 years, had abdominal cramps, diarrhea and general prostration. Three had enlarged spleens. Paradysentery of the Flexner bacillus type was found in two. One of the children died following convulsions. Another series of eleven cases is cited in which the condition was traced to a meat

stew of which all the patients had partaken. All the patients had vomiting, diarrhea and enlargement of the spleen. The bacillus of mouse paratyphoid B was recovered from the stools of four. The meat stew, which had been made three days previously and left standing in the family apartment, also contained the bacillus of mouse paratyphoid B.

Such outbreaks occur yearly in New York City after religious holidays that make it necessary to have all food cooked in advance. The most common organism found is the bacillus of mouse paratyphoid B. AIKMAN, Rochester, N. Y.

THE EFFECT OF TROPICAL SUNLIGHT ON THE DEVELOPMENT OF BONES OF CHILDREN IN PUERTO RICO. MARTHA M. ELIOT, U. S. Dept. of Labor, Children's Bureau, publication no. 217, 1933.

This is a somewhat extended consideration of the article on the same subject by Eliot and Jackson in the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**46:** 1237 [Dec.] 1933). EDITOR'S ABSTRACT.

A NUTRITIONAL DISEASE OF CHILDHOOD ASSOCIATED WITH A MAIZE DIET. C. D. WILLIAMS, Arch. Dis. Childhood **8:**423 (Dec.) 1933.

A description is given of a disease occurring in the Gold Coast Colony in children of both sexes between the ages of 1 and 4 years. The disease appears to take from four to twelve months to declare itself. There is a history of deficient breast feeding, the only supplementary food used having been a preparation of maize.

The lesions of the skin are extensive, well marked and characteristic. They may be accompanied by slight edema of the extremities. The mucous membranes are often inflamed and ulcerated, and the saliva is frequently acid. In the late stages corneal ulcers are often present. The nervous system shows persistent irritability, but the reflexes are normal.

The temperature is irregular, and the pulse rate is rapid. There is no great anemia, and the blood shows no leukocytosis. The Wassermann reaction is negative, and no parasites are to be found in the blood, except when there is associated malaria. There is a tendency to vomiting, and in chronic cases wasting may be severe. Diarrhea occurs and becomes persistent in the later stages. The stools show undigested food, but no ova or parasites. The liver and spleen may be enlarged. The respiratory system is not necessarily affected. The urine may show a trace of albumin.

Nothing characteristic is seen post mortem, except a fatty, almost diffluent liver. There may be some degeneration of the kidneys.

Treatment consists in the administration of an adequate diet rich in accessory substances. KELLY, Milwaukee.

SO-CALLED ACIDOSIS IN CHILDREN. REGINALD MILLER, Brit. M. J. **2:**1103 (Dec. 16) 1933.

The author outlines what is called cyclic vomiting and gives a brief historical résumé of the literature. He points out the various theories and dwells on the chronic "pandemic" type of the disorder. He thinks that ketosis or ketonuria is the result and not the cause. He points out that the cyclic vomiting does not occur when a ketogenic diet is given. He believes that indicanuria and a poor reserve of glycogen in the liver, with resulting poisoning of the liver, are the cause, and that back of this is intestinal toxemia. ROYSTER, University, Va.

CHRONIC INTESTINAL INDIGESTION IN CHILDHOOD. WILFRED SHELDON, M. J. Australia **2:**595 (Oct. 28) 1933.

The author lists this condition as one of the common disturbances of childhood, but calls attention to the fact that it is not the same as celiac disease, although

the two terms are at times used synonymously in this country. The three main factors in the etiology are: (1) unsuitable food, especially when too high in starch or bulky residue, (2) mismanagement which leads to poor dietary habits and (3) chronic nasopharyngeal infection. The symptoms always include definite impairment of the nutrition, with intestinal disturbances varying from eructations to mucous colitis. Treatment includes careful regulation of exercise and rest, a bland diet and prolonged observation.

TENNEY, Madison, Wis.

THE TREATMENT OF DIARRHOEA IN CHILDHOOD. RICHARD W. B. ELLIS, Practitioner **131**:642 (Dec.) 1933.

The author stresses the fact that diarrhea is a symptom usually of greater importance in infancy than in later childhood. As to etiology, the following classification is made: (1) infective, (*a*) enteral (caused by contaminated milk, utensils used in feeding or food) and (*b*) parenteral (this may arise from an infection to which the infant is susceptible); (2) environmental (due to hot weather, high humidity, ventilation, chilling or irregular feeding), and (3) dietetic (due to a diet high in carbohydrate or to vitamin deficiency).

Diarrhea may give rise directly to various degrees of dehydration, collapse and disturbance of the acid-base balance. Ellis points out the importance of treating every patient under general management as a potential source of danger to others and emphasizes the need for precautions in regard to isolation. General hygiene and care of the skin and clothing are given special attention. The treatment of dehydration is considered at length, including the administration of fluids by mouth and by the subcutaneous, intraperitoneal and intravenous routes. Careful consideration is also given to feeding and treatment with drugs. The subject of celiac disease is also presented, and a suitable diet is outlined. Nervous diarrhea and its treatment are described.

In conclusion, the author mentions the importance of the inspection of stools by the physician and the use of the laboratory for diagnostic aid when blood and mucus are present.

SAPPINGTON, San Francisco.

VITAMINS IN CLINICAL MEDICINE. S. J. COWELL, Practitioner **132**:15 (Jan.) 1934.

From the premise that man has to be taught that his food must contain an adequate supply of essential accessory substances the author proceeds to a brief description of the chief sources and clinical uses of the vitamins. In connection with vitamin D, he states that cereals actively interfere with the calcification of bones and teeth; hence, the greater the proportion of the diet that is furnished by cereals the more important it is that a liberal supply of vitamin D should be given.

The attention of physicians is called to the fact that in certain types of patients and in certain circumstances it may be of great importance to insure the completeness of diets in all known respects.

SAPPINGTON, San Francisco.

DIET AND DISEASE IN CHILDREN. ALAN MONCRIEFF, Practitioner **132**:72 (Jan.) 1934.

The author proposes to illustrate how scientific knowledge of nutrition may be translated in terms of everyday experience. Certain foods and nutritional factors of importance in childhood are discussed, namely: milk, vitamins and minerals. There follows a brief account of certain disorders especially amenable to prevention and treatment by dietetic measures, namely. gastro-enteritis, allergic disorders, acidosis, cyclic vomiting, epilepsy, pyelitis, constipation, "mucous disease," diabetes, fevers, celiac disease and nephritis. The appropriate treatment for diabetes is touched on lightly.

SAPPINGTON, San Francisco.

A Study of Growth and Development. R. M. Fleming, Privy Council, Medical Research Council, Spec. Rep. Ser. no. 190, 1933.

Successive annual observations were made on the same children in order to observe the course of growth in individual cases. More than four thousand boys and girls of Welsh stock were measured for the following anthropometric characters: height, length of the head, breadth of the head, cephalic index, biauricular breadth, auricular height, bizygomatic breadth, bigonial breadth, nasomental height, nasio-alveolar height, vertex-mentum height, circumference of the head, minimum frontal diameter and nasal index. The pigmentation, the color of the eyes and the shape of the forehead were also studied. The data are classified in five divisions on the basis of the cephalic index, and various physical, physiologic and psychologic characteristics of these groups are discussed. LeMaster, Evanston, Ill.

Milk for Infant Feeding. P. Lereboullet, Nourrisson **21**:273 (Sept.) 1933.

The various regulations in different countries regarding the production and handling of milk intended for infant feeding are reviewed and discussed, especially those in America concerning certified milk. Unless a clean, safe, fresh milk can be guaranteed, the author believes that the evaporated milks and milk powders will have to be relied on for infant feeding. McClelland, Cleveland.

Digestive Ferments in the Urine. G. Surányi and L. Veszelszky, Nourrisson **21**:296 (Sept.) 1933.

It has been shown that digestive ferments, especially rennin, can be found in the urine of many infants. Such ferments are much more common and are excreted in larger amounts in infants who are artificially fed than in those receiving breast milk. This is thought to be nature's attempt to produce an excess of ferments in infants carrying the greater digestive burdens. McClelland, Cleveland.

Precocious Lactation. Fulconis, Nourrisson **21**:310 (Sept.) 1933.

A report is made of a woman who began lactating copiously during the seventh month of her second pregnancy. She had had a similar experience during the first pregnancy. The quantity of breast milk was sufficient before parturition to nourish adequately four athreptic infants. After parturition the supply was adequate for the mother's own baby. From this the author argues that lactation is due to a hormone secreted by the gravid uterus. McClelland, Cleveland.

Acupuncture for Habitual Vomiting. M. Lavergne, Nourrisson **22**:95 (March) 1934.

Acupuncture as recommended by the Chinese was used by Lavergne in fifteen cases of habitual vomiting in infants. The ages of the babies varied from 20 days to 7 months. Lavergne insists that success depends largely on making the puncture accurately at the point described in the substernal fossa. Successful results are recorded in eight cases. McClelland, Cleveland.

Malt Preparations in Infant Feeding. R. Mathieu, Nourrisson **22**:129 (May) 1934.

Malt extract acts as a laxative, owing to the high content of maltose. Preparations of maltose and dextrins vary in their intestinal effect, depending on the maltose-dextrin ratio. Those containing high percentages of the disaccharide maltose are laxative and increase fermentation, while, conversely, those containing high percentages of the polysaccharide dextrins are constipating and putrefactive. The use of the various preparations depends on the feeding conditions which have to be met. The disaccharide lactose behaves like other disaccharides and is laxative. McClelland, Cleveland.

BREAST FEEDING. ALVARO BAHIA, Arch. de pediat., Rio de Janeiro **6**:459 (Dec.) 1933.

The author reviews the infant welfare movement and pleads for a more thorough understanding on the part of mothers of the desirability of nursing their infants.

SANFORD, Chicago.

USTILAGINISM OF MAYERHOFER AND ITS RELATION TO INFANTILE ACRODYNIA. BRANKO DRAGISIC, Arch. f. Kinderh. **101**:30 (Dec. 19) 1933.

The term "ustilaginism of Mayerhofer" refers to a disease of infants caused by eating corn-meal or bread containing spores of Ustilago maydis, a moldlike parasitic fungus. Clinically, the disease resembles infantile acrodynia, but is differentiated by the demonstration of spores of Ustilago maydis, the absence of sweating, dry desquamation of the skin, warm hands, hypotonia and a normal leukocyte count. The clinical course of three cases of ustilaginism and two cases of acrodynia seen by the author are described. Feeding maize containing spores to mice produced symptoms and pathologic changes similar to those seen in children. Acrodynia, pellagra, chronic arsenic poisoning, ergotism and ustilaginism cause similar symptoms and cutaneous eruptions, but should be clearly differentiated, since each has a different etiology.

LEMASTER, Evanston, Ill.

VALUE OF HONEY IN THE NUTRITION OF CHILDREN IN THE FORM OF THE SO-CALLED HONEY CURES. ANTON ROLLEDER, Arch. f. Kinderh. **101**:244 (March 31) 1934.

Rolleder fed half of a group of fifty-eight school boys honey twice daily for six weeks and used the other half for controls.

Among the boys receiving honey seventeen showed an increase in hemoglobin, and nine showed a decrease, while nineteen gained weight and only three lost weight. In the group of boys who were not given honey eight showed an increase in hemoglobin, and sixteen showed a decrease, while fourteen gained and six lost weight. The author believes that the general appearance, muscle tone, color and behavior of the boys who were fed honey were definitely improved.

LEMASTER, Evanston, Ill.

EFFECT OF FAT ON THE BLOOD SUGAR CURVE. GERTRUD PAASCH and HERBERT SCHOENFELD, Monatschr. f. Kinderh. **59**:181, 1934.

Some observers have reported that the ingestion of fat causes a rise in blood sugar. The authors repeated these experiments in twelve children, giving 50 Gm. of olive oil by mouth and determining the blood sugar at half hour intervals for four hours. They failed to confirm the work of the other investigators that the curve resembles that following the ingestion of dextrose.

GERSTLEY, Chicago.

INFLUENCE OF CHOLESTEROL FEEDING IN FOWLS ON THE EGGS. T. MIYAMORI, J. Pediat. (Tokyo), Nov. 20, 1933, no. 402, p. 1911.

The author noted a slight increase in the number of eggs laid by hens which were fed 1 Gm. of cholesterol daily by mouth, but no noticeable effect was seen in the weight, the percentage of cholesterol, the absolute cholesterol content, the water content and the dried ash content of the eggs.

KATO, Chicago.

UNLIMITED FEEDING OF COW'S MILK IN INFANTS. S. SHIKUMA, J. Pediat. (Tokyo), Nov. 20, 1933, no. 402, p. 1949.

The author shows favorable results of unlimited feeding of cow's milk diluted with rice water with the addition of from 3 to 5 per cent cane sugar in nine infants. The infants were fed as much as they desired six or seven times daily. The largest

amount consumed within a day was 1,960 cc. of a half and half mixture by a male infant 4 months old who weighed 5,460 Gm., or 202 calories per kilogram of body weight.

KATO, Chicago.

CHRONIC DISTURBANCES OF FEEDING IN OLDER CHILDREN. J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **3**:67 (Nov.) 1933.

A short survey of the chronic disturbances of feeding in older children and, more extensively, the symptomatology of celiac disease are given; the different methods proposed for the treatment of the disease are discussed.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the New-Born

PREVENTING LOSS OF WEIGHT IN THE NEWBORN. I. NEWTON KUGELMASS, RUTH E. BERGGREN and MILDRED CUMMINGS, New York State J. Med. **33**:1365 (Dec. 1) 1933.

The initial loss of weight is due to dehydration and semistarvation. While "it is sanctioned universally without physiologic foundation, it can be prevented by the administration of a solution consisting of 6 per cent gelatin (p_H 6.2), 3 per cent dextrose and 0.5 per cent sodium chloride at two hour intervals throughout the 24 hour cycle immediately after birth. The gelatin hydrates blood and tissues; it raises body heat by virtue of its specific dynamic action; and reduces the clotting time. Dextrose brings the new-born hypoglycemia to normal. Sodium chloride raises the initial low blood chloride and favors hydration."

AIKMAN, Rochester, N. Y.

ANEMIA OF THE NEWBORN; CASE REPORT. A. B. SCHWARTZ, Wisconsin M. J. **33**:98 (Feb.) 1934.

Reports of the rather profound anemia which develops rapidly in the first two weeks of life are infrequent. Schwartz reports the case of an infant who at first appeared quite normal, but who took feedings poorly and showed pallor on the seventh day of life; petechial hemorrhages of the skin developed on the tenth day. At this time the hemoglobin was 30 per cent; red cells numbered 1,090,000 and leukocytes, 46,550, with 51.5 per cent polymorphonuclears and 1.5 per cent myelocytes. There were 26 nucleated red cells to each 200 white cells. A blood transfusion and the administration of a liver preparation in rather large doses resulted in a normal count within three weeks.

JANNEY, Wauwatosa, Wis.

CEREBRAL HEMORRHAGE IN THE NEW-BORN. H. NERSON, Nourrisson **22**:21 (Jan.) 1934.

As evidence that all cases of cerebral hemorrhage in the new-born are not due to trauma, data are presented in the case of a septipara, aged 42, who was delivered by cesarean section on account of hemorrhage due to placenta praevia. The baby weighed 3,070 Gm. and was normal in appearance. When it was delivered the fetal heart was beating, but no spontaneous respirations ensued. Necropsy revealed a cerebral hemorrhage in the posterior horn of the lateral ventricle on the left. There was no evidence of congenital syphilis in the baby, and the mother had a negative Wassermann reaction.

MCCLELLAND, Cleveland.

RITTER'S DISEASE. H. ELIAS and M. SCHÄCHTER, Clin. pediat. **16**:47 (Jan.) 1934.

Elias and Schächter report three cases of so-called Ritter's disease in the new-born. They characterize this condition by its evolution through three stages: (1) a primary, generalized, scarlatiniform erythema, (2) a secondary stage of

extensive and confluent bullae and (3) generalized exfoliation with a typical Nikolsky sign. It is fatal in the majority of cases. Evidence for considering this disease a separate entity seems to be meager. Epidermolysis exists in pemphigus neonatorum. Typical pemphigus may develop into Ritter's disease, and an epidemic of the latter condition may be preceded by or associated with the former.

DOOLEY, Kent, Conn.

ERYTHROLEUKOBLASTOSIS, ICTERUS GRAVIS AND CONGENITAL ANASARCA. R. PETERS, Beitr. z. path. Anat. u. z. allg. Path. **92**:531, 1934.

Peters presents a study of a case of icterus gravis and one of congenital anasarca in children of the same mother. The infant with anasarca, a boy who died immediately after birth, was born two and one-half years after the infant, a girl, who died on the third day after birth of icterus gravis. Two children born previously were normal, as were both parents. Marked erythroleukoblastosis in the liver, spleen and kidneys was common to both the children who died. The author tabulates and discusses seventy-five cases of congenital anasarca and fifty-two of icterus gravis in which there was microscopic examination. With Schridde, von Gierke and others, he considers both conditions to be manifestations of the same congenital maldevelopment, the outstanding characteristic of which is erythroleukoblastosis. Icterus gravis is frequently associated with ascites, and congenital anasarca with jaundice. Congenital anasarca is held to be the more severe grade of the process. The infants are usually born prematurely and are dead at birth or die shortly thereafter. In icterus gravis the duration of pregnancy is longer and may be normal; the child lives for a few days, and some children probably recover.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

Acute Infections

RELIABILITY OF SKIN TEST IN EVALUATING THE POTENCY OF SCARLET FEVER STREPTOCOCCUS ANTITOXIN. WALTER E. KING and JOHN H. CONLIN, Arch. Pediat. **50**:727 (Oct.) 1933.

Experiments on six thousand, four hundred and sixty-three human subjects, involving twenty-five thousand, two hundred and forty-eight individual injections, were carried out in an effort to determine whether the commonly used skin test on a human subject affords a reasonably accurate and satisfactory method for evaluation of the potency of scarlet fever streptococcic antitoxin. The writers conclude that the present method is entirely accurate and reliable.

WADDELL JR., University, Va.

EPIDEMIC CEREBROSPINAL MENINGITIS IN CHILDREN; A CRITICAL REVIEW OF FORTY-FOUR CASES. ADOLPH G. DE SANCTIS, M. Clin. North America **17**: 103 (July) 1933.

This article is a résumé of present-day knowledge of the etiology, symptoms and other features of epidemic cerebrospinal meningitis. The experience of the author is that the conservative use of serum gives better results than intensive treatment. Serum is given intraspinally not oftener than once daily. Injected serum remains in the subarachnoid space for about twenty-four hours, and more frequent drainage will probably remove cells that have been stimulated to a high degree of phagocytic power. Serum should be given intravenously and intramuscularly only in cases which show persistent meningococcemia and in cases of meningococcic septicemia without meningitis. Severe and even fatal reactions have followed the intravenous injection of serum. Daily doses of serum should be given until there is clinical improvement and until two successive specimens of spinal fluid show an absence of organisms. Thereafter, it is given every other day until practically all symptoms have disappeared. Later, drainage alone may be necessary to relieve increasing intracranial pressure. The therapeutic test

appears at present to be the only reliable method for the determination of the curative value of any serum. In the event that no improvement is noted after several injections of one kind of serum, another should be substituted.

EUGENE SMITH, Ogden, Utah.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASE. Pub. Health Rep. **49**:221 (Feb. 16) 1934.

For the period from Dec. 31, 1933, to Jan. 27, 1934, influenza and measles showed an increase over the corresponding periods of the preceding year. Influenza showed an increase of two thousand cases over the number of cases reported in 1932. This increase was in the South Atlantic and South Central areas. Measles showed an increase of 2.4 times that of the number of cases reported in 1933 and the highest incidence for the last six year period. The average mortality rate from all causes was 12.6 per thousand.

SANFORD, Chicago.

INFANTILE SEPSIS AND ITS NUTRITIONAL EFFECTS. A. G. OGILVIE, Arch. Dis. Childhood **8**:413 (Dec.) 1933.

Thirty-one cases of septic infection in infants were studied. Infantile sepsis is an important cause of ill health and death among babies and is a potent source of infection in institutions.

As in any other disease, the prognosis varies as the resistance of the patient and the size and virulence of the infective dose, but patients with subacute cases do much better than those with acute cases, and the longer a child survives the greater its chance of ultimate recovery. The general mortality appears to be about 30 per cent. The portal of entry is perhaps most frequently the respiratory tract, although definite conclusions in regard to this point have not been attempted.

The impression is that of a basal septic focus which produces general toxic symptoms and periodic embolic lesions until the patient acquires sufficient resistance to overcome the infection or until death occurs.

Emphasis is laid throughout on the pronounced effect of this disorder on the digestive processes and the general nutrition and on the difficulty in diagnosis to which this may give rise. It has long been recognized that severe digestive and nutritional effects are produced by septic infection in infants, but there has been insufficient recognition in the literature of the insidious character often assumed by the disease and of the ease with which the cause may be overlooked.

KELLY, Milwaukee.

ENCEPHALOMYELITIS OF MEASLES. C. C. and A. ELLIOTT, Brit. M. J. **2**:734 (Oct. 21) 1933.

The authors report a case of encephalomyelitis which came on at the height of an eruption of measles, with complete recovery, and comment on the theories as to the pathology.

ROYSTER, University, Va.

OBSERVATIONS ON WHOOPING-COUGH AND ITS TREATMENT BY VACCINES. R. W. COCKSHUT, Brit. M. J. **2**:819 (Nov. 4) 1933.

The author thinks that pertussis vaccine has a definite therapeutic value and states that he has seen dramatic results follow its use. He believes that failure to get results comes from giving too small doses of the vaccine. His doses are much larger than those usually recommended.

ROYSTER, University, Va.

THE DURATION OF PASSIVE IMMUNITY TO DIPHTHERIA. E. G. MUNRO JONES and J. D. KERSHAW, Brit. M. J. **2**:969 (Nov. 25) 1933.

The authors tested a series of persons in a ward for patients with scarlet fever, one hundred in all, carrying out the Schick test at various periods after the injec-

tion of 500 minims of diphtheria antitoxin. They conclude that immunity is secured in 97.9 per cent of patients under 10 years of age and that such immunity lasts for at least fourteen days and in the majority of cases extends to twenty-one days.

ROYSTER, University, Va.

EXTREME HYPERPYREXIA IN MEASLES. K. M. PURVES, Brit. M. J. **1**:801 (May 5) 1934.

An underweight child, aged 3 months, had measles, during which the temperature reached 109.2 F. There were convulsions, and the child died.

ROYSTER, University, Va.

COMPARATIVE ASPECTS OF LOUPING-ILL IN SHEEP AND POLIOMYELITIS OF MAN. W. S. GORDON, Brit. M. J. **1**:885 (May 19) 1934.

Louping ill in sheep is described, with an outline of the characteristic features. Comparison is then made with poliomyelitis in man; the nature of the virus and the epidemiology in both diseases are discussed. No claim is made that the two conditions are identical.

ROYSTER, University, Va.

EXTENSIVE DIPHTHERITIC PARALYSIS WITH COMPLETE RECOVERY. JAMES B. SAMSON, Brit. M. J. **1**:895 (May 19) 1934.

A 13 year old girl was admitted to the hospital with severe diphtheria, faucial in type, with enlarged cervical glands and a number of other complications. Before admission the family physician had injected 32,000 units of diphtheria antitoxin. On admission to the hospital 18,000 units more was given intravenously and 30,000 intramuscularly, making a total of 62,000 units given intramuscularly and 18,000 given intravenously. A detailed account of the course is supplied. The patient showed extensive paralysis, including involvement of the diaphragm, the respiratory condition apparently approaching that of immediate death.

On the fifty-second day of the disease 12,000 units of diphtheria antitoxin was injected intramuscularly, and between the fifty-fifth and sixty-sixth days all evidences of paralysis had cleared up.

The author does not claim that the diphtheria antitoxin given so late in the disease did any good, but calls attention to the fact that there was rapid improvement after its administration.

ROYSTER, University, Va.

SCARLET FEVER. GEORGE F. DICK and GLADYS H. DICK, Edinburgh M. J. **41**: 1 (Jan.) 1934.

The Cameron Prize Lecture of the University of Edinburgh was delivered on Oct. 6, 1933, by the Dicks of the University of Chicago. A short résumé of the history of scarlet fever and an account of the early attempts at prevention and at isolation of the causative organism are first given. The investigation by the Dicks began in 1912, two centuries after the time of Sydenham, who named the disease. The authors narrate briefly their own experience in producing experimental scarlet fever and describe the confirmation of their results by various workers in other parts of the world. The method of preparation of the sterile filtrate and its use in skin tests are described. The writers emphasize five conclusions from their work: 1. Scarlet fever streptococci can be identified. 2. Quarantine can be controlled by cultures on blood agar plates. 3. Skin tests give needed information about susceptibility. 4. Susceptible persons can be actively immunized. 5. A specific antitoxin has been prepared for the treatment, prevention and diagnosis of scarlet fever.

Thirteen pages are devoted to this lecture. This presents the most modern conception of scarlet fever and represents the great advance in the study of the etiology, diagnosis, prevention and treatment of the disease. The lecture should be read in its entirety.

NEFF, Kansas City, Mo.

THE CONDUCT AND VALUE OF SCHICK TESTING AND ACTIVE IMMUNIZATION AGAINST DIPHTHERIA DURING AN OUTBREAK. C. S. BARBOUR, M. J. Australia **2**:363 (Sept. 16) 1933.

Barbour reports that active immunization of susceptible children during an epidemic of diphtheria produced immediate protection against clinical diphtheria in contacts and exerted a definite influence in bringing about the subsidence of the outbreak. Immunization was produced by two subcutaneous injections of anatoxin in amounts of 0.5 and 1 cc. at intervals of three weeks. In two cases sufficient immunity was given by the first 0.5 cc. of the anatoxin. In general, however, the speed of development of immunity seemed to vary with the person. The anatoxin caused no general reaction in young children; in older persons it caused no general reaction and no local reaction of serious import if the dosage was regulated by previous skin tests. Even small doses caused the development of some immunity, as was determined by the Schick test, but it was not until the first decimal point was reached (0.1, 0.2, etc.) that immunity was appreciable with only two injections.

GONCE, Madison, Wis.

SOME EXPERIMENTAL WORK ON POLIOMYELITIS. R. SOUTHBY and M. MCKIE, M. J. Australia **2**:404 (Sept. 23) 1933.

In experiments with monkeys the authors found that the neutralizing power of pooled normal serum of adults against the virus of poliomyelitis was between 30 and 40 per cent that of convalescent serum. A few experiments seemed to indicate that monkeys immune to a virulent strain possessed a greater degree of immunity to the potent Rockefeller virus than did those immune to a weaker strain of local virus and suggested that in further work on the relationship between Australian and American strains the question of the virulence of the virus, as well as that of definite immunologic difference, must be taken into consideration.

GONCE, Madison, Wis.

PARAPLEGIA DURING WHOOPING COUGH IN A CHILD AGED THREE. E. PICHON and H. CAMBESSÉDÈS, Arch. de méd. d. enf. **37**:33 (Jan.) 1934.

The authors report a case of pertussis in a girl, aged 3 years, which was complicated during the third week by paraplegia on flexion, of uncertain origin. After a few days of fever and increasing pain in the lower limbs, the child assumed a fixed position, the legs being flexed rigidly on the thighs and the thighs on the abdomen, in the so-called *chien de fusil* posture. All attempts at extension brought excruciating pain; the patient was able to rest on the right side only; the reflexes were normal, but there was incontinence, probably due more to fear of pain than to paralysis of the sphincters. The sensorium was not affected until late in the disease. Examination by deep punctures and roentgenograms eliminated disease of the hip joint. Ankle clonus, together with a bilateral Babinski sign, was found as the disorder progressed. The diagnosis rested between paraplegia of medullary origin (Ollivier-Babinski type) or one of cortical origin (Alajouanine type). The results of spinal puncture seemed to favor the latter, and although autopsy was refused the writers believe the condition to have been encephalitis superimposed on whooping cough.

AMESSE, Denver.

VELOCITY OF RED BLOOD CELL SEDIMENTATION FOLLOWING IMMUNIZATION WITH TOXOID (RAMON). GABRIELLO AMORE, Pediatria **41**:1484 (Dec.) 1933.

The author studied the sedimentation time of the red blood cells during vaccination with the anatoxin of Ramon and found a temporary decrease. He concludes that: (1) The introduction of toxoid causes a modification (slowing) of the sedimentation speed and (2) this slowing or modification is in direct proportion to the quantity of toxoid introduced.

SIGNORELLI, New Orleans.

TREATMENT OF PERTUSSIS, WITH SPECIAL REFERENCE TO INJECTION OF MOTHER'S BLOOD. U. DE GIRONCOLI, Riv. di clin. pediat. **32**:69 (Jan.) 1934.

The use of pertussis vaccine has not given as good results in practice as one would hope for. The author much prefers treating pertussis by the injection of maternal blood into the child, especially the infant.

Twenty cases of pertussis in infants aged from 25 days to 23 months are reported; from 5 to 10 cc. of citrated mother's blood was injected intramuscularly on one, two or three occasions. There was rapid remission of the disease in twelve cases, improvement in five and no benefit in three. HIGGINS, Boston.

SCARLET FEVER AND FOURTH DISEASE (FILATOV-DUKES DISEASE). MAGLIANO GIOVANNI, Riv. di clin. pediat. **32**:289 (March) 1934.

After a discussion of the literature on fourth disease and a description of sixteen cases seen by the author in Genoa, the following conclusion is reached: Fourth disease is probably a modified type of scarlet fever and should be so regarded in respect to prophylaxis and isolation. The name "scarlatinal syndrome of Dukes-Filatov" is proposed. HIGGINS, Boston.

INFLUENCE OF CARDIAC CHANGES IN FATAL DYSENTERY IN INFANTS. PAUL VON KISS and ROBERT MARTYN, Arch. f. Kinderh. **101**:67 (Jan. 31) 1934.

Repeated electrocardiographic tracings were made in nine cases of fatal dysentery in infants. In six of these the heart was examined grossly and histologically after death to correlate the anatomic observations with the electrocardiographic evidence. In the acute stage of dysentery the cardiac changes were chiefly functional, consisting of tachycardia and dilatation of the coronary veins. Occasionally, in the acute stage definite anatomic changes in the heart, such as degenerative changes in the conduction system and the adjacent musculature, could be seen. In the chronic form of dysentery the electrocardiogram and histologic examination showed atrophic changes, with gradual failure of nutrition of the heart muscle. LEMASTER, Evanston, Ill.

IS A FAVORABLE EFFECT TO BE EXPECTED FROM BLOOD TRANSFUSION IN DIPHTHERITIC CARDIAC DISTURBANCES? PAUL VON KISS, Arch. f. Kinderh. **101**:84 (Jan. 31) 1934.

In two cases of malignant diphtheria with toxic myocarditis blood transfusion not only failed to save the patients but seemed to cause a change for the worse The author believes that when circulatory failure occurs in diphtheria it is due to cardiac damage rather than to peripheral vascular changes; consequently, blood transfusion is contraindicated, because it causes additional work for a heart already damaged and overworked. LEMASTER, Evanston, Ill.

TETANUS FOLLOWING THE ADMINISTRATION OF TETANUS ANTITOXIN. H. HANKE, Deutsche Ztschr. f. Chir. **242**:62 (Nov. 23) 1933.

The author describes two fatal cases of tetanus complicating a generalized infection from eight to ten days after the original injury, at which time the usual injections of tetanus antitoxin were given. As a result he emphasizes the need of repeated administration of tetanus antitoxin. This should be given six or seven days after the first injection, as protection from the first dose begins to diminish after that period. The dangers of anaphylactic shock are emphasized, and reference is made to the use of tetanus antitoxin derived from cattle serum instead of horse serum for patients sensitive to horse serum. The repeated administration of tetanus antitoxin is particularly indicated in cases in which no healing of the wound has occurred and those in which infection has been carried deep into the tissues. Badly contaminated fractures and wounds dressed with drains

going deep into the tissues are especially dangerous from the standpoint of tetanus. The proper primary care of the wound is also of the utmost importance. In selected cases, such as those of persons subject to repeated injuries which may be contaminated by soil, active immunization against tetanus by means of toxoid should be considered.

The abstractor is particularly interested in the mention of tetanus antitoxin derived from cattle serum. It is greatly to be regretted that such serum is not commercially available in this country, where progress in the practical application of the lessons learned from anaphylaxis and allergy has been so great in recent years.

GLASER, Rochester, N. Y.

DIPHTHERIA. S. WOLFF, München. med. Wchnschr. **80**:1813 (Nov. 17) 1933.

Wolff reports two cases of diphtheria with unusual localization, one of which was that of a girl, aged 2½ years, who was treated for four weeks for gonorrheal vulvovaginitis. A few days after she became ill her brother showed balanitis, which was also considered a gonorrheal infection. After three weeks the girl had difficulty in swallowing and walking. At the time of admission to the hospital there was paralysis of the palate and extremities. The diagnosis of diphtheria was confirmed bacteriologically and by the good therapeutic result following serotherapy in both cases.

The author reports other cases which were treated successfully with serum: A girl, aged 9 years, who had untreated sore throat, showed paralysis of the muscles of accommodation. Six weeks later, 15,000 units of diphtheria antitoxin was given intravenously. Vision was greatly improved within a week and was normal within three weeks. Another girl, aged 12 years, after untreated sore throat, showed signs of paralysis and dyspnea and began to vomit. Eight days later she was brought to the city for treatment, but was so weak that she could not get out of the carriage. Examination revealed a cyanotic child with paralysis of the palate and all the extremities and an irregular, weak pulse. The child was given 20,000 units of diphtheria antitoxin intravenously and the same dose intramuscularly. After ten days she was well.

The serum should not be given subcutaneously in the treatment of diphtheria. Intravenous and intramuscular injections are advised and should be given as early in the disease as possible. In severe cases 50,000 units may be given.

Several German authors have advocated the treatment of diphtheria with normal horse serum. This may prove disastrous, as in one case cited by the author.

BRAHDY, Mount Vernon, N. Y.

RELAPSE IN PRIMARY SCARLET FEVER. I. REIDERMANN, Wien. klin. Wchnschr. **45**:1477 (Nov. 25) 1932.

Reidermann deals with three cases of undeniable scarlet fever in children in which the initial complex of symptoms of scarlet fever was repeated on the fifteenth, seventeenth and twenty-second days respectively. In all three cases principal scaling, and in two cases the typical complications—rheumatoid arthritis, lymphadenitis and otitis—had begun. The children were isolated, living with their mothers in separate rooms with separate entrances from the floor. Aside from the physician in charge, they received no visitors.

The fact that the initial complex of scarlet fever may repeat has been noted in the literature; however, physicians know little about it. During the past few years, certain physicians of scarlet fever divisions, in conversations with their colleagues, told of cases in which some children who were turned over to them by the most esteemed pediatricians "first sickened" with scarlet fever on reaching the division. A short time ago it was not unusual for a physician to sit in the prisoners' dock accused of sending a child into the scarlet fever division who there contracted this disease. Although facts of this nature are not frequent, yet in the mass material of hospitals they must appear striking.

In the large, excellently prepared statistical study made by Gabriel and Zischinski, it was noted that the yearly incidence of recurrent scarlet fever varied from 0.42 to 6.83 per cent; however, from 1922 to 1929 the percentage of recurrent cases remained fairly steady at between 2.49 and 3.43 per cent.

Among the cases cited by Gabriel and Zischinski are those of five children in whom the appearance of scarlet fever was observed three times during their sojourn in the hospital.

The question of the cause of the relapse is debatable. A new infection from the outside is to be considered (Pospischill, Fankoni), as is autoreinfection (Ferraris-Wysz).

On the basis of their mass of material, Gabriel and Zischinski assume that in the majority of cases a relapse appears as the direct result of a new infection from the outside. They believe that the moot question as to whether or not a relapse is a new infection from the outside can be decided only if there is opportunity to observe closely such a case in an exceptionally isolated patient. The three cases cited by Reidermann establish that a reappearance of the initial scarlet fever during the secondary period of the disease is possible when the possibility of reinfection from the outside has been absolutely excluded. ABT, Chicago.

THE BLOOD PICTURE OF TYPHOID FEVER IN CHILDREN. Y. FUKABORI, J. Pediat. (Tokyo) **389**:1915 (Oct. 20) 1933.

Fukabori reports a summary of his studies of forty-six patients with typhoid fever. He found absence of leukopenia in 13.1 per cent of them and these showed only mild symptoms clinically. All those with severe symptoms showed leukopenia. The severity and rapidity with which leukopenia appeared seemed to depend on the age of the patient; as a rule, the younger the child the milder and slower the appearance of this phenomenon. The number of basophils decreased during fever and increased with defervescence. The eosinophils disappeared during the height of the disease. The neutrophils increased in number during the prodromal stage with a distinct shift to the left. The toxic granulations in the neutrophils also corresponded with the progress of the disease. The lymphocytes showed the inverse variations. The number of monocytes showed a slight decrease at the beginning, gradually increasing with the course. KATO, Chicago.

DIFFERENTIAL DIAGNOSIS OF ACUTE EXANTHEMS IN CHILDHOOD. T. HALBERTSMA, Maandschr. v. kindergeneesk. **3**:26 (Oct.) 1933.

This article is a survey of the symptoms of the acute exanthems of childhood and a discussion of their value in differential diagnosis.

VAN CREVELD, Amsterdam, The Netherlands.

NURSING IN THE HOSPITAL IN SCARLET FEVER. D. HERDERSCHÉE, Maandschr. v. kindergeneesk. **3**:247 (March) 1934.

Until last year nearly all patients with scarlet fever, who, for the most part, had mild cases, were sent to the hospital in Amsterdam. The frequency of the disease was not restricted, however. Present economic conditions have helped to change this system, and now only those patients are sent to the hospital in whom the disease is severe or for whose admission special social reasons exist. The arguments for and against nursing patients with scarlet fever in the hospital and in the home are given. VAN CREVELD, Amsterdam, The Netherlands.

EXAMINATION OF THE BLOOD AND BACTERIOLOGIC INVESTIGATION AS MEANS OF AN EARLY DIAGNOSIS OF PERTUSSIS. J. A. VAN HAAFTEN, Maandschr. v. kindergeneesk. **3**:102 (Dec.) 1933.

In the catarrhal stage of whooping cough there is often leukocytosis combined with lymphocytosis. However, this typical blood picture may be totally absent

during the catarrhal stage and become distinct only during the convulsive stage. The bacteriologic investigation in whooping cough (cough-plate method) makes for an early diagnosis and can be easily performed; when the results are positive, this is an absolute guarantee of the correctness of the diagnosis. The bacteriologic investigation has, however, several important difficulties.

VAN CREVELD, Amsterdam, The Netherlands.

SEPSIS CURED BY A TURPENTINE ABSCESS. A. VON WESTRIENEN, Maandschr. v. kindergeneesk. **3**:277 (April) 1934.

A girl, aged 6 years, suffering from sepsis, showed a remarkable diminution in the number of polymorphonuclear cells after the appearance of the turpentine abscess and the fall in temperature.

VAN CREVELD, Amsterdam, The Netherlands.

EPINEPHRINE IN DIPHTHERIA. D. HERDERSCHÊE, Nederl. tijdschr. v. geneesk. **77**:5572 (Dec. 16) 1933.

During the treatment of patients with diphtheria there may occur two phases in which one may be inclined to make use of epinephrine. One of these, which does not correspond directly with the diphtheria intoxication, is serum disease; the other is postdiphtherial disturbance of the circulation. When shock or collapse results from the application of serum, epinephrine may be used, in the author's opinion, when, before the injection of serum, there were no distinct symptoms of disturbed circulation. The author warns, however, against the use of epinephrine and other stimulants in cases of diphtheria with disturbances of circulation; then rest is required primarily.

VAN CREVELD, Amsterdam, The Netherlands.

WHY IS THE MALARIA IN HOLLAND RESTRICTED TO SOME DISTRICTS? P. H. VAN THIEL, Nederl. tijdschr. v. geneesk. **78**:997 (March 3) 1934.

To explain the phenomenon of anophelism without malaria in Holland not only the difference between the ways of hibernation of the large-winged and small-winged Anopheles maculipennis must be considered, but also the difference in the numbers of Anopheles in regions with and without malaria. The latter factor must be active especially between the end of July and the beginning of September, in which a great number of malarial infections probably occur.

In contradiction to the generally accepted assumption that the spring peak of malaria (so far as it occurs before June) is caused by infections acquired in the foregoing autumn, which have remained latent, the author argues that by further investigation it will be shown that at least a fraction of these infections have been acquired in July and August. This assumption is founded chiefly on the anamnesis of cases of malaria which occurred in the period of 1920-1922 in the malaria-free town of Leyden and agrees with experience in other European countries. The question at what time of year malaria is most often acquired in Holland may be answered best by practitioners in malaria-free regions, who often can by accurate inquiry ascertain when their patients with malaria have resided in a contaminated region.

It is further asked whether frequent incidence of malaria for years in some places might be explained by the presence in scanty numbers of Anopheles labranchiae, which is considered dangerous in southern Europe, as has already been found in Germany. This was investigated in July 1933 at Franeker, Holland. Gnats were found which might be determined as Anopheles labranchiae, in houses as well as in stables, not only at Franeker but also in about the same frequency at Dronryp and Haarlemmerliede, where malaria occurs far less frequently. Therefore, these forms are of no epidemiological importance. It would, however, be better not to label them labranchiae, but to investigate the variability in the structure of the air spaces of the eggs. Of the distinctive features of labranchiae, this is the best and is characteristic only of the small-winged Anopheles maculi-

pennis (variation atroparvus), the species which prevails practically alone in the regions of Holland in which malaria is found.

VAN CREVELD, Amsterdam, The Netherlands.

COWPOX IN MAN. J. A. C. SCHEPEL, Nederl. tijdschr. v. geneesk. **78**:1855 (April 28) 1934.

In Friesland, the northern part of Holland, where there are many cattle, cowpox is met with comparatively often. The symptoms in several cases in milkers and milkmaids are described. Further contamination is now prevented by prophylactic vaccination of both cattle and men.

VAN CREVELD, Amsterdam, The Netherlands.

Chronic Infections

EFFECTS OF THEELIN AND THEELOL IN LATENT TETANY. FRANZ MATHIEU and B. O. BARNES, Am. J. Physiol. **105**:172 (July) 1933.

In four parathyroidectomized female dogs with latent tetany the calcium level in the blood was lowered further with the administration of theelin and theelol. Less change was noted in the phosphorus level, only one dog showing a definite rise when the calcium was very low. Active tetany did not follow the administration of the female sex hormone.

NOURSE, Cleveland.

UNDULANT FEVER (BRUCELLA INFECTION) IN CHILDREN. JOHN F. LANDER, J. Michigan M. Soc. **32**:109 (Feb.) 1933.

Lander desires to impress on the medical profession the fact that infection with Brucella occurs in children much more frequently than is generally believed.

He cites the case histories of children varying in age from 17 months to 11 years, all of whom showed a positive skin reaction to the nucleoprotein of Brucella abortus and negative phagocytosis for this organism. Negative results of physical and laboratory examinations were noted.

A vaccine from Brucella abortus in four doses (one of 0.3 cc., one of 0.5 cc. and two of 1 cc. each) was given intramuscularly at three day intervals. A slight increase in fever was noted following the first injection in some of the cases. This quickly disappeared, and subsequent injections were not followed by febrile disturbance. Ten days after the last injection, each patient's blood showed a high phagocytic activity for Brucella abortus in vitro, with rapid convalescence following.

CAREY, Detroit.

DEMONSTRATION OF GROWTH OF TUBERCLE BACILLI. W. T. MUNRO, Edinburgh M. J. **41**:168 (March) 1934.

At a meeting of the Scotch Tuberculosis Society the author demonstrated the different characteristics in growth of human and bovine types of tubercle bacilli. Growths of the bovine type of tubercle bacilli were shown in sputum obtained directly, in sputum procured by gastric lavage in a child 5 years old, in cerebrospinal fluid and in urine. The colony is smooth, moist and flat, in contrast with the larger, rounded, sometimes wrinkled growth produced by the human type. On Löwenstein's medium the growth is usually present by the fourth or fifth day.

NEFF, Kansas City, Mo.

SOME ASPECTS OF TUBERCULOSIS OF THE NERVOUS SYSTEM. EDWIN BRAMWELL, Edinburgh M. J. **41**:195 (March) 1934.

The author emphasizes tuberculomas of the nervous system. He questions whether the frequency of tuberculous tumor in the cerebellum of children may

not be related to the frequency of tuberculous otitis at this period of life and be due to the direct extension of infection.

NEFF, Kansas City, Mo.

PROBLEMS OF RESEARCH IN TUBERCULOSIS. A. SALUSBURY MACNALTY, Edinburgh M. J. **41**:207 (March) 1934.

This article contains an interesting discussion on bacterial allergy and immunity as they relate to tuberculosis.

Of especial interest is the British experimental conclusion regarding the question of B C G. MacNalty states that much remains to be done before one can feel that a safe and effective immunizing agent has been perfected which will prevent tuberculosis. Both dead and living vaccines produce only transient immunity.

NEFF, Kansas City, Mo.

GRANULOSIS RUBRA NASI AND HEREDITARY SYPHILIS. M. PAVIA, Riv. di clin. pediat. **32**:308 (March) 1934.

The author reports a case of granulosis rubra nasi in a boy, aged 8 years. Although this disease of the skin and vasomotor system is usually associated with tuberculosis, in this child skin tests and physical examination gave negative results for that disease. Hereditary syphilis is probably an etiologic factor in this child's condition.

HIGGINS, Boston.

TREATMENT OF TUBERCULOUS MENINGITIS WITH ROENTGEN RAYS. C. WIENER, Jahrb. f. Kinderh. **138**:249 (March) 1933.

Twelve patients treated according to the technic described by von Bókay, (*Jahrbuch für Kinderheilkunde* **135**:69 [March] 1932), became much more ill and died.

CLAUSEN, Rochester, N. Y.

IMPORTANCE OF LATENT OPEN PULMONARY TUBERCULOSIS IN THE SMALL CHILD. B. KEMKES, Ztschr. f. Gesundhführ. **1**:7 (Jan.) 1934.

Work done by Scandinavian and German pediatricians has called attention to the fact that children with positive tuberculin tests and few or no signs in the lungs may, nevertheless, have tubercle bacilli in the contents of their stomachs. Some authors have deduced from this that all such children should be isolated. This, of course, would require complete reorganization of hospitals and sanatoriums and would entail great expenditure. The author admits the facts mentioned, but does not believe that the experience of institutions has shown that the so-called latent cases are dangerous as a source of contact. He therefore advises the following procedures:

1. All small children admitted into institutions should be tested for their tuberculin reaction.

2. Children with positive reactions should be studied roentgenologically.

3. If anything is found in the lungs at this procedure, children should not be admitted to open wards or institutions.

4. Roentgenologic examination should be repeated at intervals.

5. Children showing positive tuberculin reactions but no other signs should be admitted to open institutions.

REICHLE, Cleveland.

THE USE OF AN ACETARSONE PREPARATION (OSARSOL) IN SYPHILIS. V. Y. KAPLUN and V. L. BORSHCHEVSKIY, Soviet. klin. **19**:244, 1933.

Kaplun and Borshchevskiy administered osarsol (a preparation similar to acetarsone) to 204 syphilitic patients; 19 had primary and secondary manifestations; 125 were in the secondary stage, and the rest in the tertiary stage. Thirty-eight received only the preparation of acetarsone; the others received the drug in

combination with mercury, bismuth or iodide preparations. The initial dose was 1 tablet of 0.25 Gm. a day, which was increased daily by 1 tablet up to 4 tablets a day. One half of the dose was given in the morning on an empty stomach and the other half before retiring. In one course of treatment 120 tablets were given. In order to avoid a cumulative effect, the course was divided into six parts, with intervals of three or four days between. This was done because it was found that already on the third day after discontinuation of the drug there were only traces of arsenic in the urine, and that on the fourth day no arsenic could be detected.

Nineteen patients received three courses, 87 patients two courses and 98 patients one course. Spirochetes disappeared from lesions in the skin after from two to five days; roseola vanished after from ten to fourteen days and papules after from twelve to fourteen days. In patients with active secondary syphilis a Herxheimer reaction was frequently noticed, particularly on the second day; such a reaction lasted for one or two days. The action of the arsenical on the Wassermann reaction was somewhat less effective than that of arsphenamine. The toxic effects were mild; they were mostly noticed in the first part of the course of treatment and disappeared in the majority of instances in spite of continued administration of the drug. Fever was an exception, and was followed in most cases by dermatitis. The dermatitis was usually urticarial or erythematous; only in one instance was there a vesicular eruption. Like the other toxic manifestations, the dermatitis was benign.

In 11 cases there was hypersensitivity, which was due not only to the acetarsone preparation but also to arsphenamine. Five patients who did not tolerate arsphenamine received the arsenic compound without injurious effects. Four patients who were sensitive to this compound tolerated neoarsphenamine. In 2 patients desensitization to the acetarsone preparation could be effected by administering small doses, starting with 0.01 Gm. Women and children were proportionately more sensitive to the drug than men. The development of a toxic manifestation, particularly dermatitis, could be foreseen a few days before absence of arsenic in the urine.

The authors believe this arsenical to be useful in peasants during seasonal work on the fields, in sailors and in patients who cannot tolerate arsphenamine or in whom arsphenamine is contraindicated.

BLOOM, New York. [ARCH. DERMAT. & SYPH.]

Internal Diseases

LOCALIZATION OF FOREIGN BODIES IN THE LUNG BY ROENTGEN EXAMINATION, WITH COMMENTS ON BRONCHOSCOPY UNDER BIPLANE ROENTGENOSCOPIC GUIDANCE. HENRY K. PANCOAST, EUGENE P. PENDERGRASS and GABRIEL TUCKER, Am. J. Roentgenol. **27**:225 (Feb.) 1932.

Two cases are reported in which it was previously impossible to furnish roentgenoscopic guidance during attempts at bronchoscopic localization of foreign bodies, because the foreign bodies could not be localized roentgenoscopically. A method that was successfully used in the two cases reported is suggested for use in localization of the foreign body and for assistance during roentgenoscopic guidance in bronchoscopic removal. Opaque markers for localization of the foreign body were used, making it possible to guide the bronchoscopist by the markers instead of the relatively nonopaque foreign body. Roentgenograms using the Potter-Bucky diaphragm should be made of every obscure and dense lesion of the lung before excluding a diagnosis of foreign body.

Dr. Tucker's summary follows: "Roentgenoscopic bronchoscopy should be biplane and should not be attempted on the patient until the bronchoscopist and the roentgenologist, working together, have perfected their cooperative technique on the narcotized living animal. Because the large blood vessels of the lung are in intimate relation to the field of manipulation in roentgenoscopic bronchoscopy, and

are not visible on roentgenoscopic guidance, fatal hemorrhage may result from slight trauma. The patient's life depends on the 'sense of touch' of the bronchoscopist. Roentgenoscopic guidance by the Pancoast-Pendergrass method has enabled us to remove, with safety, foreign bodies that could not be localized by ordinary methods. Roentgenoscopic bronchoscopy is of value in the diagnosis and treatment of certain disease conditions and in the evacuation of cysts and interlobar collections."

STULIK, Chicago.

AN ORIGINAL METHOD OF ESTIMATING KIDNEY FUNCTION BY MEANS OF THE ROENTGEN RAY IN INTRAVENOUS UROGRAPHY. E. C. CARHART, Am. J. Roentgenol. **27**:234 (Feb.) 1932.

The roentgen opaqueness of a sample of urine passed thirty minutes after an intravenous injection of methiodal is checked against a series of six tubes of graduated concentrations. It is considered that approximately 40 per cent of the injected methiodal should be eliminated in the urine in thirty minutes. To be sure that there is no residual urine in the bladder another film of the bladder is made immediately after collecting the first sample. The results obtained by control methods with intramuscular injection of phenolsulphonphthalein correspond accurately. The advantages of the method are ease and simplicity of administration, painlessness, usually more speed, less expense for the patient and no after-symptomatology, and the renal function can be accurately estimated at the time of urography.

STULIK, Chicago.

UNUSUAL PNEUMONIAS ASSOCIATED WITH THE ASPIRATION OF FATS AND OILS IN THE LUNGS. J. W. PIERSON, Am. J. Roentgenol. **27**:572 (April) 1932.

Two infants, 4 months of age, who had been getting oil for a considerable time, died of extrapulmonary infection after a period of illness during which pulmonary symptoms and signs did not dominate the clinical picture. All tests for tuberculosis were consistently negative. The roentgen findings presented an accurate picture of gross pathologic changes in the lungs, and indicated much more extensive pulmonary involvement than was brought out by the clinical examination. The reports on the pathologic changes revealed large quantities of fatty material in the lungs, and chronic pneumonia and fibrosis. Fats and oils often reach the alveoli of the lungs when they are given to children orally or nasopharyngeally. They collect in the lungs and are associated with chronic pneumonias and fibrosis. The widespread use of oils in pediatrics offers a large potential source for this condition. The presence of fatty material in the lungs produces an interesting roentgen picture, but no pathognomonic signs are offered. The communication is presented with the hope that it may stimulate roentgenologists to make observations that will aid in the diagnosis of this condition.

STULIK, Chicago.

AURICULAR FIBRILLATION IN CHILDHOOD: REPORT OF CASE TREATED BY QUINIDINE SULPHATE. SAMUEL F. JENKINS and NOLAN OWENS, Arch. Pediat. **50**:479 (July) 1933.

The case of a child with auricular fibrillation, who was treated with quinidine sulphate, is reported.

WADDELL JR., University, Va.

THE URINARY TRACT IN INFANTS AND CHILDREN AS SEEN FROM A PEDIATRIC VIEWPOINT. A. W. CHAPMAN, Arch. Pediat. **50**:538 (Aug.) 1933.

The writer believes that medical men as a class do not fully appreciate the importance or the frequency of disorders in the urinary tract of infants and children. This fact is especially to be regretted since diagnostic methods available for the acquisition of information pertaining to the urinary tract in adults are

also applicable to infants and children. The more common infections of the urinary tract and their symptomatology are reviewed, and their etiology is discussed, as well as methods of therapy.

Chapman believes that a large proportion of patients suffering from infections of the urinary tract coming under the head of pyurias can be successfully treated by physicians, but stresses the fact that in a relatively small number of cases if a diagnosis is not made and the patient is not given surgical aid he will either die or suffer the effects of prolonged renal damage. It is of paramount importance that physicians recognize and differentiate between these benign and serious forms.

WADDELL JR., University, Va.

MEDIASTINAL LYMPHOSARCOMA. SYDNEY NUSSBAUM, Arch. Pediat. **50**:561 (Aug.) 1933.

A case of mediastinal lymphosarcoma of the lymphatic variety was presented and its close resemblance to leukemia discussed. In the writer's particular case the initial increase of the tumor following roentgen therapy caused compression of the trachea and large vessels of the mediastinum sufficient to cause asphyxiation.

WADDELL JR., University, Va.

PRIMARY CARCINOMA OF THE LUNG IN A CHILD. J. MURRAY BEARDSLEY, Canad. M. A. J. **29**:257 (Sept.) 1933.

A case of primary carcinoma of the lung in a child is presented, the first metastatic lesion being noted when the patient was 10 months old. The metastatic lesion appeared in the lumbar region and was removed. Histologic examination showed that it was an adenocarcinoma. Six months later there was a recurrence of the growth along the line of the scar.

Roentgen examination of the lungs at this time showed normal pulmonary fields. Eighteen months later pulmonary signs developed, and the child died. Autopsy showed a soft necrotic tumor filling almost the entire left lung.

MOORE, Omaha.

IS SPORADIC GOITER DEPENDENT UPON GENOTYPICAL FACTORS? E. MEULENGRACHT, Endocrinology **17**:383 (July); 392 (Aug.) 1933.

A family is described in which six sisters, a maternal aunt and a daughter had goiter. Two similar families whose cases are recorded in the literature are cited. The author feels that the accumulative occurrence of goiter in these families indicates that the disease is entirely or partly dependent on genotypical factors, since there was no demonstrable influence of external conditions. He considers it probable that the apparently isolated instances of sporadic goiter are also of this origin.

JACOBSEN, Buffalo.

X-RAY SHADOWS IN GROWING BONES PRODUCED BY LEAD: THEIR CHARACTERISTICS, CAUSE, ANATOMICAL COUNTERPART IN THE BONE AND DIFFERENTIATION. E. A. PARK, D. JACKSON, T. C. GOODWIN and L. KAJDI, J. Pediat. **3**:265 (Aug.) 1933.

A careful study of the changes in the bones produced by lead poisoning in children is presented. The appearance in the roentgenogram of the shadows at the ends of the growing bones is described, and the underlying histopathologic changes are discussed in detail. The differential diagnosis of other conditions causing similar shadows in the bones is considered, such as medication with viosterol, transverse lines due to arrested growth, phosphorus poisoning, syphilis, scurvy and administration of bismuth. The two striking features seen in the histologic preparations of the ends of the growing bone are the persistence of the cartilaginous intercellular substance of the cartilage, which contains lead as well as calcium, and the huge giant cells lying between the trabeculae.

LEMASTER, Evanston, Ill.

DILATATION AND HYPERTROPHY OF THE HEART IN INFANCY DUE TO PARENCHYMATOUS MYOCARDITIS. F. E. KENNY and S. SANES, J. Pediat. **3**:321 (Aug.) 1933.

Two cases of marked dilatation and hypertrophy of the heart observed in infants, aged 1 year and 6 months, respectively, are reported. In each instance histologic examination revealed different stages of diffuse parenchymatous myocarditis. Cardiac symptoms and enlargement of the heart first appeared following bronchopneumonia in one case and following acute stomatitis in the other.

LEMASTER, Evanston, Ill.

THE MEASUREMENT OF ABERRANT DEVELOPMENTAL GROWTH: I. THE MANAGEMENT OF PREADOLESCENT DISTURBANCE. THEODORE T. ZUCK, J. Pediat. **3**:424 (Sept.) 1933.

The author cites illustrative cases from his studies of aberrant growth to demonstrate the rate of progress before and during treatment with preparations of the endocrine glands. The retardation of these children is shown by their weight, height and general appearance and by roentgen examination of the bones, at various intervals of time. Under the proper therapy, with substances from the thyroid and pituitary glands in these cases, the acceleration of maturation is definitely followed by repeated examinations.

LEMASTER, Evanston, Ill.

CONGENITAL OSTEOSCLEROSIS. GEORGE E. ROBERTSON, J. Pediat. **3**:439 (Sept.) 1933.

A case of congenital osteosclerosis is reported and the condition discussed. The patient was an Italian girl 10 months old. From the age of 3 months the child had received 3 teaspoonfuls of 10D cod liver oil daily. Besides the denseness of the bones and the obliteration of the normal trabeculations, the child had a palpable spleen and definite anemia, with a high percentage of immature white and red blood cells. The values of the blood phosphorus were low. The author favors the view that the osteosclerosis is primary and the changes in the hematopoietic system are secondary.

LEMASTER, Evanston, Ill.

MYELOSARCOMATOSIS. RALPH H. KUNSTADTER, J. Pediat. **3**:479 (Sept.) 1933.

A case considered one of myelosarcomatosis is reported. The child, 6½ years old, had multiple malignant tumors histologically resembling undifferentiated myeloid tissue. There were many atypical white cells in the blood. The differential diagnosis of the disease is considered in relation to the findings in this case.

LEMASTER, Evanston, Ill.

HYPERTROPHIC PYLORIC STENOSIS IN TWINS. ARTHUR E. VARDEN, J. Pediat. **3**: 493 (Sept.) 1933.

Hypertrophic pyloric stenosis in monozygotic twin boys is reported, and similar cases found in the literature are reviewed and analyzed. Although data on the subject are meager, the author believes that the weight of evidence at present points to the theory that the source of hypertrophic pyloric stenosis is congenital.

LEMASTER, Evanston, Ill.

ROCKY MOUNTAIN SPOTTED FEVER IN SOUTH CAROLINA. O. B. MAYER, J. South Carolina M. A. **2**:209 (Sept.) 1933.

The third authentic case of this disease occurring in South Carolina is reported by O. B. Mayer. The history, symptoms and signs were typical of Rocky Mountain spotted fever. The Weil-Felix reaction of the blood was positive. The patient, aged 12, had a furunculosis before making a complete recovery.

WESTON JR., Columbia, S. C.

PROGRESS IN PEDIATRICS: THE PARATHYROIDS. JOHN LOVETT MORSE, New England J. M. **208**:843 (April 20) 1933.

The parathyroid hormone mobilizes the calcium stores of the body into the blood; in increased amounts it withdraws an excessive amount of calcium from the bones and does harm; if a proper amount is lacking, the blood calcium falls, and tetany may result.

The hormone is supposed to affect only the diffusible portion, i. e., that not combined with protein, and therefore theoretically its administration is not indicated in nephrosis with low blood calcium, although cases of nephrosis have been reported in which the edema has been materially diminished by the administration of parathyroid extract. Experimental studies by Collip indicate that oral administration is ineffective, i. e., that the extract should be given intravenously or subcutaneously. The symptoms of hypercalcemia in dogs caused by excessive amounts of parathyroid appeared as follows: anorexia, vomiting, diarrhea, musclar weakness and lassitude, respiratory distress, passing of blood by bowel, bloody vomit and finally collapse.

Lowenburg and Ginsburg reported a case of acute hypercalcemia as the result of excessive doses of parathyroid extract and calcium gluconate given by mistake for six days to a 5 year old boy for the control of hemorrhage. The first symptom was vomiting, which persisted; then gradually increasing weakness and lethargy developed until the patient was unable to sit up and there were practically no voluntary movements. The temperature was high and irregular; the blood calcium was 19.6 mg., and the serum phosphorus, 4.4 mg. Recovery occurred after withdrawal of medication, and the blood calcium returned to 10 mg.

Osteitis fibrosa cystica (Recklinghausen's disease) is believed to be due to chronic hyperparathyroidism; improvement or cure results from removal of the parathyroids.

The author believes that parathyroid extract should be used only as an emergency treatment for tetany, the proper treatment of the underlying rickets being much more important.

GENGENBACH, Denver.

THROAT MANIFESTATIONS OF THE BLOOD DYSCRASIAS. EDLEY H. JONES, South. M. J. **26**:550 (June) 1933.

Some blood dyscrasias present such marked manifestations in the throat that otolaryngologists may be consulted before conference is held with an internist.

These dyscrasias may be suspected from the results of simple and common laboratory procedures.

In all suspected cases adequate laboratory examinations should be made.

In all cases, particularly preoperative ones, the history should contain definite information regarding any previous hemorrhages; further, in all preoperative cases the bleeding and coagulation time should be determined.

SCHLUTZ, Chicago.

THE TREATMENT OF HOOKWORM AND OTHER INTESTINAL HELMINTH INFECTIONS WITH HEXYLRESORCINOL UNDER FIELD CONDITIONS IN CENTRAL AMERICA. DANIEL M. MOLLOY, South. M. J. **26**:575 (July) 1933.

The author reports treatment of ancylostomiasis with hexylresorcinol. A total of 1,784 treatments were administered in different cases, and no toxic symptoms from the drug were observed. Slight gastric irritation occurred occasionally, but nausea was rare and vomiting did not occur. On account of the action of hexylresorcinol on the gelatin of capsules, the drug is best administered in sugar-coated pills. Full therapeutic (1 Gm.) doses of the drug removed from 65 to 72 per cent of the hookworms, under field conditions. The efficacy of the drug is greatly lessened if it is not given on an empty stomach, or if food is taken shortly after administration. Clearing the intestinal tract of extraneous matter by a preliminary purge would probably increase the efficacy of the drug, and this would be a recommendable procedure in the treatment in individual cases.

In the treatment of infections by Ascaris the drug is probably without an equal. From 93 to 98 per cent of the ascarids harbored by the persons treated were expelled by a single treatment. In the treatment of whipworm infestations the drug appears to be less effective than earlier reports indicated. It would, however, appear to be the most effective drug to use against this parasite at the present time.

The administration of a purge two hours after the drug is administered lessens its anthelmintic effect. On account of its delayed action, phenolphthalein may be administered simultaneously with the drug without lessening its efficiency against hookworms and Ascaris. If saline purgatives are employed, they should not be administered until several hours later, preferably the following morning.

In the treatment of ancylostomiasis, a single dose of hexylresorcinol lessens the burden of worms to the extent that the patient is relieved of most of the symptoms. It does not, however, entirely eliminate the danger to others, since the majority of persons treated still harbor a sufficiently large number of worms to be considered "carriers." In campaigns which are being conducted for the purpose of reducing mass infection, a second treatment (preferably with some anthelmintic which possesses a more selective action against hookworm, like tetrachlor-ethylene, carbon tetrachloride or thymol) would seem to be indicated.

SCHLUTZ, Chicago.

THE EFFECT OF DIET ON THE WORM BURDEN OF CHILDREN INFECTED WITH NECATOR AMERICANUS AND ASCARIS LUMBRICOIDES. C. F. AHMANN and L. M. BRISTOL, South. M. J. **26**:959 (Nov.) 1933.

This study was undertaken to determine the effect of a well balanced diet on the worm burden of children infected with Necator americanus and Ascaris lumbricoides. The method of Stoll for making ova counts was found to be accurate to within less than 5 per cent and was shown to be a satisfactory method for determining the worm burden of infected persons. The reduction in incidence was 100 per cent for ascaris, and the trend was toward reduction for hookworm. In one instance there was a marked reduction in the hookworm ova count following the improvement in diet, while in the other case the change was less pronounced.

SCHLUTZ, Chicago.

PNEUMOCOCCAL INFECTION IN INFANCY AND CHILDHOOD. J. W. S. BLACKLOCK and K. J. GUTHRIE, J. Path. & Bact. **36**:349, 1933.

The pathology and bacteriology of pneumococcic infections in infants and children of the hospital class are discussed. In cases of acute respiratory disease, throat swabs were used for isolating the pneumococcus as sputum is not easily obtained in the young child. In 38.6 per cent of healthy children, pneumococci were found in the throat, 96.7 per cent of these being group IV strains. The accuracy of the results of the examination of the throat swab in a series of cases of pneumonia was confirmed in 88.5 per cent. Some of the cases of pneumonia which did not come to autopsy could not be definitely classified. In a few cases the lesions in the lungs, when examined histologically, showed characters of both lobar pneumonia and bronchopneumonia; such mixed types were most frequent in the second year of life. Pneumococci from 140 cases of pneumonia were typed, 9.3 per cent belonging to the fixed types (chiefly types I and II) and 90.7 per cent to group IV. The mortality rate of the fixed type infections was 38.5 per cent and of the group IV infections, 40.9 per cent. In adult cases of lobar pneumonia investigated simultaneously in the same city, 73 per cent were due to types I, II and III pneumococci and only 27 per cent to group IV. The bacteriology of bronchopneumonia was studied post mortem in a series of cases. Pneumococci were found in 85.5 per cent, streptococci in 7.3 per cent, influenza bacilli in 6.1 per cent and Staphylococcus aureus in 1.1 per cent. Pus from the pleura in 114 cases of empyema yielded pneumococci in 68.4 per cent, streptococci in 17.5 per cent and

other organisms in 14 per cent. The mortality was slightly higher in pneumococcic than in streptococcic empyemas. Pneumococci were typed in 66 cases of empyema, and 30 belonged to type I, 1 to type II and 35 to group IV. The incidence of fixed type infections rose with the age of the child, group IV strains predominating in the empyemas following bronchopneumonia in early childhood. The mortality rate in fixed type infections was 32.2 per cent, and in group IV infections, 54.3 per cent. Of 27 cases of primary pneumococcic peritonitis, 24 (88.9 per cent) were in girls and 3 in boys. In 10 of the 11 female children examined at autopsy, the peritoneal lesion was most acute in the pelvis. Of the 3 boys, only 1 was examined post mortem, when no lesion except peritonitis was found. In 13 cases type I, and in 2 cases type II pneumococci were isolated from the peritoneal exudate. Pneumococcic peritonitis secondary to pneumonia was rare, occurring in only 2.4 per cent of the cases, and in these the thoracic lesions were severe. Pneumococcic meningitis occurred most frequently as a sequel to acute otitis media and was primary in only 17.6 per cent of the cases studied. Of the pneumococci isolated from the cerebrospinal fluid, 84.2 per cent belonged to group IV. Purulent otitis media was present in 21.1 per cent of 2,000 consecutive autopsies; the pneumococcus was the predominating organism in the pus from this lesion. The commonest complication in a series of cases of pneumonia examined post mortem was acute otitis media. In 33 cases of acute disease of the middle ear pneumococci were typed, 93.9 per cent being group IV strains. Infection was due to group IV pneumococci in 70.6 per cent of a series of surgical lesions (arthritis, orchitis and acute abscesses). On arranging the 292 strains of pneumococci isolated from various acute lesions according to the type of coccus and the age of the patient, it was found that the percentage of infections with fixed types was much greater in older children than in those under 3 years.

AUTHORS' SUMMARY. [ARCH. PATH.]

THE INFLUENCE OF THE ENDOCRINE SYSTEM IN BLOOD DISORDERS. DOUGLAS HUBBLE, Lancet **2**:113 (July 15) 1933.

This paper consists of two parts. In the first, the author outlines the effect of the hormones of the thyroid gland, the suprarenal glands and the pituitary gland on hematopoiesis. In the second part the attempt is made to trace by fact, analogy and theory, evidence of endocrine disorder in the hyperplasias and hypoplasias of the blood the etiology of which is still obscure.

It is shown that the hormone of the thyroid gland stimulates the production of red cells and lymphocytes and depresses the output of granulocytes; that the supradrenal cortical hormones of the suprarenal glands stimulate the production of granulocytes and possibly also of red cells, and that the basophil cells of the anterior lobe of the pituitary gland stimulate all types of circulating cells, giving rise to a clinical picture of polycythemia. It is possible that the hormone from the anterior lobe of the pituitary gland produces this leukopoietic result indirectly through the thyroid and the suprarenal cortex. It is suggested that in hyperplasias and hypoplasias of the circulating blood cells, a primary disorder of the endocrine system is the dominant etiologic factor. The clinical parallelism between exophthalmic goiter and chronic lymphatic leukemia is displayed, with particular reference to Friedgood's work on the response of the basal metabolic rate, the pulse rate and the cell count in lymphatic leukemia to treatment with compound solution of iodine. It is concluded that the cause of lymphatic leukemia is a primary dysfunction of the thyroid gland.

It is suggested that an excess of a suprarenal cortical hormone is responsible for myelogenous leukemia, and it is pointed out that polycythemia is a cardinal sign of hyperplastic conditions of the anterior lobe of the pituitary gland. Two hypoplasias of the marrow are considered, agranulocytic angina and aplastic anemia, and further evidence is reviewed which suggests an endocrine etiology for them also.

LANGMANN, New York.

A Case of Adolescent Hypertension with Excretion of an Adrenaline-Like Substance in the Urine. Clifford Hoyle, Lancet **2**:230 (July 29) 1933.

The case of a 14 year old boy is cited; he was admitted to the hospital for observation because of high systolic blood pressure. He played the usual games without any discomfort and except for measles at 2, doubtful chorea at 7 and chronic tonsillar enlargement requiring tonsillectomy at 10, his medical history was unimportant.

The positive findings were as follows: The arterial blood pressure in the upper and lower extremities was increased, ranging between 210 and 150 systolic. Both radial arteries and both brachial, facial, dorsalis pedis and posterior tibial arteries were easily palpable and unduly thickened. The cardiac impulse was abnormally forcible, and the first sound at the mitral area and the aortic second sound were accentuated. There were no murmurs. The pulse rate, at rest, was usually between 70 and 80, but varied with the blood pressure and at times rose to about 100.

A teleroentgenogram showed enlargement of the heart as a whole and particularly of the left ventricle. An electrocardiogram showed that the function was normal. Clinical and laboratory investigation failed to throw any light on the origin of the hypertension, beyond excluding chronic renal disease, congenital stenosis of the aortic arch and those gross endocrine disturbances which occur in association with medullary or cortical tumors of the suprarenal glands or basophilic tumors of the pituitary gland.

Further investigation of this problem consisted in the examination of the cerebrospinal fluid for pressor activity.

On further study it was found that in the urine were being excreted considerable quantities of some pressor substance with a physiologic action on the cardiovascular system similar to that of epinephrine and its allied pressor bases. It is suggested that the condition may be an example of high blood pressure resulting from an acquired or inborn error of metabolism. Langmann, New York.

Calcium Therapy in the Treatment of the Allergies and Its Use in the Form of "Afenil." I. Maxwell and D. Zacharin, M. J. Australia **1**:642 (May 27) 1933.

Maxwell and Zacharin treated twenty patients with allergy who had not been helped by other methods of treatment by intravenous injections of afenil, a double compound consisting of 1 molecule of calcium chloride (31.6 per cent) and 4 molecules of carbamide (68.4 per cent). The injections were given two or three times a week, and the number of injections varied up to fifteen. Forty per cent of the patients maintained some improvement for a period of six months or longer, and 15 per cent, for three months only. Gonce, Madison, Wis.

A New Intradermal Reaction in Ankylostomiasis. A. B. Vattuone, M. J. Australia **1**:645 (May 27) 1933.

Vattuone reports that the intradermal injection of an antigen prepared from ancylostomas gives an immediately positive local reaction in affected patients and carriers and no reaction in persons who are free from infection with hookworm. Gonce, Madison, Wis.

Endocarditis with Emboli in a Child with Recovery. G. H. Rossdale, Proc. Roy. Soc. Med. **26**:1019 (June) 1933.

A girl of 6 years was admitted to the hospital in April 1930 and discharged in July 1932. The illness commenced with pain in the left foot, the ankle joint being red and inflamed. There were also pain in the right hand, headache and a systolic murmur at the apex. There were fourteen periods of pyrexia, two prolonged and more severe than the rest. The condition of the child during the second period of pyrexia was so grave that death seemed inevitable. During the

course of the illness the ankles, wrists, hips and shoulders were affected, and erythematous nodules appeared on the shins and an erythematous rash over the body and limbs. There was considerable wasting. A blood culture was sterile. Antistreptococcus vaccine was given in doses of 10 cc. during November 1930, as well as an autogenous vaccine (streptococcus) made from the stools. The temperature did not rise after May 1932, and there was a steady improvement until the child left the hospital in July. The hips were still stiff, but the child got about with a certain amount of freedom. WILLIAMSON, New Orleans.

GASTROMEGALY. REGINALD LIGHTFOOT, Proc. Roy. Soc. Med. **26**:1020 (June) 1933.

The case reported was that of a girl of 12 years. She had suffered for four and a half years with attacks of vomiting and abdominal pain. The stools were loose, frequent and pale in color. Her legs became so weak that she had to be carried up and down stairs. On examination she was found to be anemic and stunted. Percussion notes showed the stomach to be enlarged. A barium meal showed the stomach much dilated and the barium shadow low in position. Peristalsis was weak, and the emptying was very slow, a residue remaining after six and a half hours. A fractional test meal showed hypochlorhydria.

WILLIAMSON, New Orleans.

PERNICIOUS BLOOD PICTURE IN AN INFANT, WITH RECOVERY. T. PEARSE WILLIAMS, Proc. Roy. Soc. Med. **26**:1268 (Aug.) 1933.

The patient, a boy of 4 months, was well until ten days previous to admission to the hospital, when diarrhea and vomiting developed. The diarrhea lasted for four days and the vomiting for two. Eight days before the attack of diarrhea, the baby had been vaccinated. The mother had noticed a few days before admission to the hospital that the baby was pale. The day after admission the spleen was found to be 1 inch (2.5 cm.) below the costal margin. The blood picture showed: hemoglobin, 78 per cent; red cells, 1,440,000; white cells, 7,500. The differential count was: neutrophils, 31 per cent; small mononuclears, 64 per cent; large mononuclears, 3 per cent, and eosinophils, 5 per cent. There were 22 normoblasts and 10 megaloblasts in a count of 400 cells. There were some megalocytes, and slight anisocytosis and polychromatophilia were seen. Further blood counts are given in the paper. The condition of the baby improved on the administration of copper, lactic acid milk and sunshine. The color improved, and the spleen receded.

WILLIAMSON, New Orleans.

ANEMIA OF VON JAKSCH. ALAN MONCRIEFF, Proc. Roy. Soc. Med. **26**:1359 (Aug.) 1933.

The case is reported of a child of 8 months with anemia. The liver and spleen were enlarged. Blood counts, made on various dates, are given in the report. Iron was the first treatment tried, then copper was added to this, but with little result. Two transfusions of blood were given during the patient's stay in the hospital. After the second transfusion, the condition of the child improved a great deal.

WILLIAMSON, New Orleans.

THE CHLOROTIC ANEMIA WITH DWARFISM AND RICKETS. LEONARD FINDLAY, Proc. Roy. Soc. Med. **26**:1365 (Aug.) 1933.

The patient, a girl of 9¾ years, was recommended to the hospital on account of knock knees. She was found to be 10 inches (25.4 cm.) below normal height for her age, and 23 pounds (10,432.6 Gm.) underweight. Examination of the blood showed anemia of the chlorotic type. The head was square, and the epiphyses of the wrists were enlarged. Roentgenograms of the wrists and knees revealed active rickets. Full laboratory tests and repeated blood counts are given in the article.

WILLIAMSON, New Orleans.

CHLOROTIC TYPE OF ANEMIA. LEONARD FINDLAY, Proc. Roy. Soc. Med. **26**:1367 (Aug.) 1933.

A case of chlorotic type of anemia was reported in a girl 11 years of age. Weekly blood counts are given in the report. These counts were made before and after the child was given pills of ferrous carbonate.

WILLIAMSON, New Orleans.

THE EFFECT OF YEAST AND WHEAT EMBRYO IN ANEMIAS: I. MARMITE, YESTAMIN, AND BEMAX IN MEGALOCYTIC AND NUTRITIONAL HYPOCHROMIC ANAEMIAS. CHARLES C. UNGLEY, Quart. J. Med. **2**:381 (July) 1933.

The author presents results obtained by feeding yeast and wheat embryo to twenty patients with anemia, observed at the Royal Victoria Infirmary and at the Massachusetts General Hospital. The methods of administration and the descriptions of the proprietary products used are clearly stated.

The results are discussed under: (1) nutritional hypochromic anemias (eight cases); (2) atypical pernicious anemia without achlorhydria (two cases); (3) addisonian pernicious anemia (ten cases).

The author concluded from his study that no effect on regeneration of hemoglobin followed the administration of massive doses of preparations of yeast or wheat germ to patients with idiopathic hyopchromic anemia.

Bemax and marmite produced a hematopoietic response in two cases of atypical pernicious anemia showing an incomplete defect in the secretion of hydrochloric acid combined with marked dietary deficiency.

Of ten patients with classic pernicious anemia treated with preparations of yeast and wheat germ, seven showed a response and three failed to show a response. Bemax gave an uncertain positive result in one case and negative results in two others. Yeast in the form of marmite or of an extract derived from marmite gave positive results in six of seven cases.

The possibility is discussed that preparations of yeast may owe their potency in treating pernicious anemia to one or more factors: (1) an extrinsic factor; (2) a breakdown product of the extrinsic factor, perhaps resulting from the interaction of this substance with an enzyme liberated during the autolysis of yeast, or (3) a substance resembling the active principle in liver.

BRADFORD, Rochester, N. Y.

CRITICAL REVIEW: ACHLORHYDRIA. T. H. OLIVER and JOHN F. WILKINSON, Quart. J. Med. **2**:431 (July) 1933.

This is an interesting and instructive review of the subject, discussed under the following headings: (1) achlorhydria in apparently normal persons; (2) achlorhydria in children; (3) achlorhydria in disease; (4) etiology; (5) the symptoms of achlorhydria; (6) the effects of gastrectomy and gastro-enterostomy on the secretion of the stomach; (7) achlorhydria associated with diseases of the blood; (8) achlorhydria and subacute combined degeneration of the spinal cord; (9) the endocrine system; (10) diseases of the pancreas; (11) rheumatoid arthritis; (12) achlorhydria in allergic and cutaneous diseases; (13) treatment of achlorhydria; (14) summary.

An extensive bibliography is appended.

BRADFORD, Rochester, N. Y.

VOLUMINOUS BRONCHOPULMONARY CYST IN A BOY OF FIFTEEN. R. DEBRÉ and H. BLINDER, Arch. de méd. d. enf. **36**:540 (Sept.) 1933.

The patient, born of healthy parents in Armenia, was almost 9 years of age when he contracted measles, which was followed by a chronic cough. Six months later he had a sudden attack of dyspnea with extreme cyanosis and collapse; he was admitted to a hospital in Constantinople, where a diagnosis of spontaneous right pneumothorax (March 1, 1922) and resulting displacement of the heart toward the left was made. It was assumed that the essential etiology in the case was concerned with pulmonary tuberculosis, aroused by the preceding attack of measles,

and a poor prognosis was recorded. The child was removed to a retreat in the forest near Constantinople and slowly convalesced to apparent recovery. In 1931, the patient accompanied his family to France and came under the observation of the authors. It was found that he still suffered from dyspnea on running or climbing or when greatly excited, but that in repose respiration was normal. Examination revealed slight distention of the right side of the chest, with exaggerated tympany and total absence of vesicular murmur and vocal fremitus on that side. The heart was displaced, the apex beat being in the sixth intercostal space beyond the nipple line. Roentgenograms were characteristic in practically every particular of pneumothorax. The probability that such a condition would persist for from six to fifteen years, however, was so remote that further studies were instituted. To eliminate tuberculosis from the pathogenesis, cutaneous tests were made and found negative; furthermore, a collapsed lung, always visible in pneumothorax, could not be demonstrated by the roentgen rays, but at the upper limit of the hemothorax one could make out fine vascular ramifications which seemed to mark the persistence of normal pulmonary tissue at this point. From the reports of cases made up to this time by Parmalee, Ribadeau-Dumas, Chabrun and others, in which this phenomenon was shown to accompany extensive pulmonary cysts, a diagnosis of the latter disease was offered.

In a review of the literature, only one other case, that of Vollmer, has been reported during life.

AMESSE, Denver.

CRANIOHYPOPHYSEAL XANTHOMATOSIS. E. LESNÉ, R. CLÉMENT and P. GUILLAIN, Arch. de méd. d. enf. **36**:546 (Sept.) 1933.

Within six months of their report of the first case of Schüller-Christian's disease found in France, these clinicians report another case observed in a girl, aged 15, a pupil of a finishing school at Yvetot. The complete and classic tetrad of this disorder was present—osseous lesions of the skull, exophthalmia, retarded development and diabetes insipidus. There were in addition serious behavioristic disturbances, bilateral deafness, supernumerary teeth and a tumor of the left mastoid region.

Schüller, in 1915, and Christian, in 1919, ascribed the syndrome to a diffuse xanthomatous reticulo-endotheliosis involving especially the cranium.

AMESSE, Denver.

PNEUMOCOCCIC UROCYSTITIS IN AN INFANT. A. VALERIO, Arch. de méd. d. enf. **36**:553 (Sept.) 1933.

While urinary infections with the colon bacillus are comparatively common in early infancy, invasions of the genito-urinary tract by the pneumococcus are unusual. Farber and Latsky have reported an instance in an infant suffering from an abscess of the kidney. Occasional cases are recorded of pneumococcic vulvovaginitis; aside from this easy route of infection the pneumococcus is more frequently a source of urinary involvement in girl babies than in boys.

The writer discusses the case of a white Brazilian child of 1½ years in whom cystitis developed four months prior to examination. There were intermittent fever, painful micturition and great loss of weight, and the urine constantly contained pus and blood. Treatment during this period was confined entirely to the exhibition of urinary antiseptics, with ample quantities of water. A catheterized specimen showed pneumococci in abundance. An autogenous vaccine was employed, and the bladder was irrigated with a weak solution of silver nitrate. Complete cure was effected in twenty days.

AMESSE, Denver.

A CASE OF OSSEOUS FRAGILITY WITH CRANIAL DEFORMITY AND BLUE SCLERAE. J. ARLABOSSE, J. de radiol. et d'électrol. **15**:92 (Feb.) 1931.

Apert, in 1928, called attention to a heredofamilial condition, the chief characteristics of which were: osseous fragility; deformity of the skull; laxity of the

ligaments; blue sclerae; auditory disorders, and impairment of electric contractility of the muscles. Since that time several similar cases were recorded in the literature. The author recently observed, in a youth 19 years of age, a marked roentgen permeability of the entire skeleton concomitant with deformity of the skull and with the presence of blue sclerae. It is interesting, however, that there were no fractures such as are usually observed in fragility of the bones (the patient indulged in active sports, such as football), and the auditory disorders, as well as the heredofamilial nature, were also absent. The case is placed in the group of osteopsathyrosis (fragility of the bones).

STULIK, Chicago.

CLINICAL AND HEMATOLOGIC STUDIES IN CERTAIN CASES OF PSEUDOLEUKEMIA INFANTUM. ITALO MARCIALIS, Clin. pediat. **15**:508 (July) 1933.

Three cases of severe anemia with splenomegaly in infants are reported. The disease had its onset without apparent or discernible cause by the end of the third month of life, and in spite of various therapeutic attempts each case ended in death within the first year of life.

In each case the author was able by means of biologic tests to exclude satisfactorily tuberculous and syphilitic infection. The blood picture in each patient was characterized by oligocythemia, poikilocytosis, anisocytosis, anisochromatic changes, intense erythroblastosis and leukocytosis. Each presented evidence of immature blood elements of the granulocytic group. These pictures were checked with studies of blood obtained by splenic puncture in one of the patients.

On the basis of the blood and histologic pictures, the author classifies these cases according to the new conception of Ferrata and Di Guglielmo, as mielosi eritroleucemica infantum.

SIGNORELLI, New Orleans.

ESSENTIAL PERMANENT ESOPHAGOSPASM IN CHILDREN. E. BENASSI, Radiol. med. **17**:1334 (Nov.) 1930.

Permanent spasm of the esophagus is extremely rare in children. The author describes two typical cases which he saw in girls, one 6 years of age and the other 7. In both, the site of spasm was at the diaphragmatic constriction of the esophagus; in all probability the condition was due to nervous hysteria. This was shown by the satisfactory results of treatment with bromide and belladonna, associated with appropriate suggestive treatment. Roentgenograms of the cases are given, which show a peculiar appearance caused by the projection of the mucous membrane contracted by the spasm into the lumen of the esophagus; this is similar to the projection of the pyloric mucous membrane at the base of the duodenum described by Busi.

STULIK, Chicago.

ULTIMATE RESULTS OF THE MEDICAL TREATMENT OF EMPYEMA. G. SANPAOLESI, Riv. di clin. pediat. **31**:385 (April) 1933.

The author reexamined thirty-seven children who had been treated for empyema by the method of Cocchi during the preceding five years. The method of Cocchi consists of thoracentesis and the injection of sodium taurocholate intrapleurally. Thirty-one of the thirty-seven children showed no signs of a pathologic condition in the chest either on physical or on roentgen examination; three showed a slight deformity of the chest but no physical signs, and three showed some pathologic condition persisting in the lungs.

HIGGINS, Boston.

UREA SECRETION CONSTANT IN CHILDREN. G. CAREDDU and M. GASPARINI, Riv. di clin. pediat. **31**:573 (May) 1933.

The author believes that the constant of Amberg is a surer index of renal function than is the constant of Apert. In glomerular nephritis of children the constant increases under much the same laws as apply in adults. In tubular or

degenerative nephritis the variations are usually insignificant. It appears that the test is as important and satisfactory for children as for adults.

HIGGINS, Boston.

DIAGNOSIS, PATHOGENESIS AND TREATMENT OF PNEUMOCOCCIC PERITONITIS, WITH A REPORT OF FIVE CASES. C. CURRADO, Riv. di clin. pediat. **31**:788 (July) 1933.

The author reports five cases of pneumococcic peritonitis; three of the patients were seen from the early stages of the disease, and two were seen a few weeks after the onset. In one case the peritonitis was secondary to pneumonia; the patient died. The other four cases were primary, and all of the patients recovered after operation.

Pneumococcic peritonitis is essentially a disease of childhood. It is usually secondary to an enteric infection.

Early surgical intervention should be avoided, as experience has shown that it is a dangerous procedure. Thus the differential diagnosis from acute appendicitis is important, especially in the early stages. The differential points are as follows:

1. In pneumococcic peritonitis, the initial rise in temperature is sudden and high (even as high as 40 C. [104 F.]), whereas in appendicitis it is slow and not very high, and the patient is occasionally afebrile.
2. The pain in pneumococcic peritonitis is severe and is not localized but diffuse. One must remember, however, that the pain in appendicitis is occasionally diffuse or even localized on the left side.
3. The abdominal rigidity is usually less marked or consistent in pneumococcic peritonitis.
4. Diarrhea is present in a majority (two thirds) of the cases of pneumococcic peritonitis.
5. Herpes labialis is more common in pneumococcic peritonitis.
6. A positive blood culture for pneumococci aids in the diagnosis.
7. The white blood count in pneumococcic peritonitis is higher, the cells averaging between 20,000 and 30,000, with about 90 per cent polymorphonuclears; in appendicitis the white cell count is usually between 10,000 and 15,000.
8. The finding of pneumococci in the vaginal secretion is of diagnostic help.
9. Exploratory puncture of the peritoneum may be resorted to, if necessary.

HIGGINS, Boston.

BEHAVIOR OF THE CAPILLARIES OF THE SKIN IN DISEASE OF THE KIDNEYS IN CHILDHOOD. G. CAREDDU and G. PAVAN, Riv. di clin. pediat. **31**:923 (Aug.) 1933.

The authors made observations on twenty-five children, of whom nineteen had glomerular nephritis, two nephrosis and four a mixed type of the two. Examination of the capillaries was made (1) by examining their structure microscopically, (2) by determining the capillary pressure (method of Frontali) and (3) by determining the fragility of the capillaries (method of Riva Rocci).

In the children with glomerular nephritis, the capillaries showed morphologic alterations, especially the venous capillaries; the capillary pressure showed marked increase over normal in thirteen cases and slight increase in four cases; the fragility was increased in eleven cases.

In the mixed type the aforementioned changes from normal were also found, but to a lesser degree.

In the children with nephrosis, the capillary pressure was practically normal, the capillaries showed only slight variation, microscopically, from normal, and in one case the fragility of the capillaries was normal and in the other slightly increased.

These observations confirm the conception of Frontali that glomerular nephritis is a manifestation of a generalized involvement of the capillaries.

HIGGINS, Boston.

A Case of an Unusual Gastric Tumor in a Child. Cihilo Aguirre and D. B. Brian, Arch. argent. de pediat. **4**:381 (June) 1933.

The authors report the case of a girl, 12 years old, in whom pain developed in the lumbar region and later epigastric pain of increasing intensity together with nausea and vomiting. Physical examination revealed a palpable, tender, poorly circumscribed tumor mass, which was movable with respiration, just above the umbilicus. There was no abnormal blood picture, and the Wassermann reaction and a tuberculin test were negative. A diagnosis of gastric tumor was made and confirmed by a roentgenogram.

An exploratory laparotomy was performed, which revealed a diffuse nodular tumor involving the pylorus and the larger portion of the stomach. Owing to the extent of involvement, neither a gastrectomy nor a gastro-enterostomy was possible. An ileostomy was done, death occurring seventeen days later. Necropsy revealed multiple disseminated, nodular tumor masses involving the gastric mucosa and submucosa and consisting of lymphoid tissue.

The authors classify this tumor in the group of "multiple lymphomas" or "lymphomatosis of the gastric mucosa and submucosa." They believe, in view of the absence of definite hematologic findings, that this may be considered as a case of "aleukemic lymphomatosis," a lesion which does not possess the destructive characteristics of a lymphosarcoma.

The authors have not found a similar case reported in the pediatric literature.

Schlutz, Chicago.

Congenital Varicosities and Intermittent Claudication in an Eight Year Old Child. J. M. Macera, M. de la Fare and Rey Sumay, Arch. argent. de pediat. **4**:404 (June) 1933.

The authors report the case of a girl, 8 years old, who from birth presented varicosities of the left leg. They originated in the form of a large bluish network on the superior and lateral aspect of the thigh and extended downward as a narrow venous tract along the outer surface of the leg to the middle toe. She had symptoms of pain on walking and even on standing for any length of time, together with paresthesia in the affected limb. There were likewise swelling and pallor of the left leg, and Buerger's maneuvers revealed circulatory changes similar to those found in thrombo-angiitis obliterans. The patient's disability had been becoming progressively worse. Resection of the internal saphenous vein with a periarterial sympathectomy resulted in complete disappearance of the patient's symptoms. The authors have found only one similar case in the pediatric literature.

Schlutz, Chicago.

Extreme Adenopathy. L. de Marval and R. G. Pons, Arch. med. d. hosp. Ramos Mejia **15**:87 (Sept.) 1932.

A patient with infectious adenopathy had an enlargement of all the upper lymph glands and a red swollen throat. The blood showed 14,000 white cells, with 78 per cent neutrophils. Glomerular nephritis eventually developed. In the differential diagnosis in such a picture lymphatic leukemia, agranulocytic angina, basillar adenitis, malignant lymphogranuloma and infectious adenitis must be considered.

Sanford, Chicago.

Laboratory Investigations in Icterus. Alejandro Chediak, Arch. de med. inf. **2**:291 (Sept.) 1933.

The author has written an interesting description of the technical methods for studying icterus, and this should be read in detail by any one interested. In brief, he finds that the most available urinary reactions for determining bile pigments are a combination of Gmelin and Grimbert's methods. Urobilin and its dye are best examined by the method of Florence and Ehrlich. Biliary salts are

tested by the reactions of Bay and Pettenkofer. Biliary salts in the stools are found by the help of the indirect method (hemokonia in the blood). Fouchet's and van den Bergh's methods are recommended for the qualitative study of bilirubin. The determination of the icteric index may lead to high values when dyes such as carotene are present in the serum. Urobilin in the blood is devoid of all clinical value, and biliary salts are not commonly tested in practice. The determination of globular stability, which is indispensable in icterus accompanied by anemia, is best made by Sanford's method. The determination of the pigmentary concentration in the duodenal juice by the sound which occurs when the liquid is withdrawn is of value. The determination of blood cholesterol is important. A test of hepatic function is frequently of value, and Bauer's method is the best of this type. A research of the etiologic factor by blood cultures, inoculations of fluid and similar measures should not be neglected. Other routine examinations, such as examination of the blood, urine and coagulation time and analysis of the stool, should be carried out depending on the clinical course of the case.

SANFORD, Chicago.

RHEUMATISM IN INFANCY. MARTINEZ VARGAS, Med. de los niños **34**:54 (Feb.) 1933.

Arthritis may occur in severe forms, for example: 1. Blennorrhagic rheumatism. The affected part is hot and red, and there is an antecedent blennorrhagia, especially in girls. Sometimes purulent ophthalmia may result. This form is of long duration and may result in ankylosis. 2. Arthritis with osteomyelitis. This type occurs in the diaphysis and is characterized by high temperature, severe pain, a rapid course and the appearance of pus. 3. Arthritis of pseudorheumatism, of which there are two varieties—that in which there is rapid suppuration, as in smallpox, and that with no suppuration, as in scarlet fever, diphtheria and erysipelas. 4. Serum disease. 5. Arthritis, with hemophilia, caused by hemorrhage in the synovial membranes.

The treatment consists of putting the child to bed clothed with flannel or wool and kept free from draughts. A liquid diet should be given during the febrile stage. Sodium salicylate, 0.5 Gm. per pound (0.5 Kg.) of body weight with sodium bicarbonate, usually gives relief from pain and fever within from twenty-four to forty-eight hours. Sulphur appears to increase the action of the salicylates. Baths are of great benefit, especially those containing sodium chloride and sulphur.

DWYER, Kansas City, Mo.

CYSTS OF THE LIVER VISUALIZED WITH THORIUM DIOXIDE. ERICH HEEGEWALDT, Rev. chilena de pediat. **3**:207 (May) 1932.

The use of thorium dioxide, which has proved to be extremely useful in urography, is recommended by the author for visualization of the liver and the spleen. The preparation is given intravenously. Approximately 12 cc. is the usual dose.

Thorium dioxide accumulates in the cells of the reticulo-endothelial system of the liver and the spleen. No toxic effects have been observed after the use of the preparation.

The author reports its use in a child, aged 6 years, affected with hydatid cysts in various organs. It was possible to visualize readily the hydatid cysts in the liver in this patient. In the opinion of the author, it should be useful in detecting cysts, tumors or malignant processes in the solid abdominal organs.

SCHLUTZ, Chicago.

CONTRIBUTION TO THE KNOWLEDGE OF STILL'S DISEASE. THERESE BERZACZY, Arch. f. Kinderh. **100**:32 (July 18) 1933.

A 5 year old boy had suffered from Still's disease for many months. The joints were painful and swollen. The lymph glands and the spleen were enlarged.

There were an irregular fever and decided anemia. The white blood count remained about 3,000 per cubic millimeter. About a month after admission to the hospital, one joint became fluctuant. It was drained, and Bacterium paratyphosum B was obtained on culture. The same organism was obtained from an inguinal lymph gland, from blood cultures and from stool cultures. It was undetermined whether Still's disease and pyemia caused by Bact. paratyphosum B coexisted or whether the paratyphoid infection was the original cause of Still's disease.

LeMaster, Evanston, Ill.

Comparative Experiments on the Effect of P-Methyl-Amino-Ethanol-Phenol Tartrate, Epinephrine, Insulin and Atropine on the Circulation and Blood Sugar. Louise Holl, Arch. f. Kinderh. **100**:47 (July 18) 1933.

In twelve well children from 5 to 13 years of age, epinephrine caused an elevation of the blood pressure, a rise in the pulse rate and an elevation of the blood sugar. P-methyl-amino-ethanol-phenol tartrate, given orally, did not influence the circulation, but caused a rise in blood sugar. In combination with atropine it intensified the effect of the atropine on the circulation, but did not affect the blood sugar. The administration of insulin and p-methyl-amino-ethanol-phenol tartrate together produced no effect on the circulation or the blood sugar.

LeMaster, Evanston, Ill.

Hematopoiesis in Adenoma of the Liver. A. Ssolowjew, Beitr. z. path. Anat. u. z. allg. Path. **88**:337, 1932.

Foci of hematopoiesis were found in a benign adenoma of the liver in a child, 18 months old, and in a malignant tumor of the liver in an infant aged 4 months. They were within dilated capillaries throughout the benign tumor and only in the more highly differentiated areas of the malignant adenoma. These foci consisted of hemocytoblasts, young red and white blood cells and megakaryocytes. The fact that in the surrounding hepatic tissue no such areas of formation of blood cells were present suggested that the endothelial cells of the capillaries of the tumor were the mother cells of the hemocytoblasts and that the anlage of these tumors was organoid and consisted of epithelial cells and capillaries.

Hellwig, Wichita, Kan. [Arch. Path.]

Histology and Etiology of Subacute Yellow Atrophy of the Liver in Children. R. Beneke, Beitr. z. path. Anat. u. z. allg. Path. **88**:538, 1932.

The author gives a detailed microscopic description of the internal organs of a child who died of severe jaundice. In the liver, there was almost complete necrosis of the parenchyma. Only a few fatty, degenerated liver cells were preserved. There was proliferation of the bile ducts and of the interlobular stroma. Chemical examination of the internal organs did not reveal any poison, and the history was not in favor of poisoning as the etiologic factor. The author hypothecates that the necrosis of the liver was possibly caused by an intensive spasm of the hepatic artery.

C. Alexander Hellwig. [Arch. Path.]

Congenital Glycogenic Hypertrophy of the Heart. W. Putschar, Beitr. z. path. Anat. u. z. allg. Path. **90**:222, 1932.

A child died at the age of 4 months of bilateral bronchopneumonia. At the age of 12 days, generalized edema was noted, but no abnormality of the heart was detected. At 13 weeks of age, it was noted that the liver was enlarged, and on admission to the hospital, marked enlargement of the heart was detected. At necropsy, the heart was found greatly enlarged, weighing 110 Gm. The wall of the left ventricle varied from 7 to 21 mm. in thickness, that of the right ventricle

from 6 to 12 mm. The liver was moderately enlarged and weighed 240 Gm. Each kidney weighed 25 Gm. The increase in the size of the heart was due to marked infiltration of the muscle fibers by glycogen. The liver cells and the epithelium of the convoluted tubules of the kidney were vacuolated by glycogen. The case is held to belong to a group of which von Gierke described two examples in 1929 as congenital glycogenic hepatorenomegaly. Von Gierke considered the condition one of abnormal glycogen metabolism, which he likened to the diseases characterized by lipoid infiltration, namely, Gaucher's disease, Niemann-Pick's disease and Hand's (Schüller-Christian's) disease. In Putschar's report there is no note of histologic examination of the pancreas. In a brief note he mentions the case of a 3 year old child in whom abnormal carbohydrate metabolism was detected during life by chemical studies. Biopsy revealed that the enlargement of the liver detected clinically was due to glycogen infiltration.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

ASTHMA IN CHILDREN. F. SARTORIOUS, Monatschr. f. Kinderh. **58**:266, 1933.

In a verbose article on asthma, the writer states that he has discovered that the disease is frequently related to eczema, that it is occasionally helped by a change of climate, and that hypodermic injections of epinephrine hydrochloride are of value.

GERSTLEY, Chicago.

THE DIAGNOSTIC SIGNIFICANCE OF DIGITAL IMPRESSIONS AND CRANIAL SUTURES IN THE X-RAY PICTURE. CARL HUNERMANN, Monatschr. f. Kinderh. **58**:415 (Aug.) 1933.

This is a clinical discussion, with roentgenograms of the juvenile skull. The study was conducted with the idea of relating the development of the digital impressions to clinical symptoms. This cannot be done. They may be absent in chronically increased intracranial pressure and may be present in a perfectly normal child. When markedly developed, they are probably a constitutional anomaly.

On the other hand, widening of the cranial sutures is a very early and reliable sign of acute increase in intracranial pressure.

GERSTLEY, Chicago.

MASTITIS ADOLESCENTIUM, A SIGN OF IMMUNITY. ERICH WALTHER, Monatschr. f. Kinderh. **58**:452 (Aug.) 1933.

In fourteen years of practice, the writer has seen twenty-eight cases of mastitis in adolescence. Four were boys and twenty-four girls. The children as a rule were languid, had little appetite and were often decidedly underweight. Contrary to the general opinion that the disease is of endocrine origin, the writer believes that it is a manifestation of occult tuberculosis. There is a reaction of the whole mesenchyme of the body to a new tuberculous infection. This, however, is a reaction of immunity, and the mastitis, which is a sign of the mesenchymal reaction, is an index of this immunity and offers a good prognosis.

GERSTLEY, Chicago.

THROMBOPENIA FOLLOWING ANGINA. E. JACOBSON, München. med. Wchnschr. **80**:26 (April 14) 1933.

Jacobson observed a patient who had vague abdominal pains followed in three days by pharyngitis and tonsillitis. The coagulation time was increased, but the bleeding time was normal (unusual). No platelets could be found. Otherwise the blood was normal. Petechiae appeared on the skin for several days. Two weeks after the onset of the sore throat there were 74,000 platelets; a month later, 191,000.

BRAHDY, Mount Vernon, N. Y.

MYOBLASTOMA. R. MEYER, Virchows Arch. f. path. Anat. **287**:55, 1932.

Meyer describes a pedunculated congenital tumor that was attached to the maxilla of a new-born infant. The tumor measured 4 by 6 by 9 cm. and protruded from the mouth; asphyxiation of the infant was prevented by the immediate removal of the mass by severing its pedicle. Twenty months after birth the child was normal. The tumor was composed of round, oval and elongated mononucleated cells that Meyer holds to be indifferent myoblasts. He describes a small tumor of similar structure in the subcutaneous tissue of the breast of a woman, aged 26 and a small nodule of the tongue of a man, aged 69. His purpose in presenting these tumors is to discuss their origin and nature, on which points he is not in entire accord with Abrikossoff, who in 1926 placed such neoplasms in a special group for which he proposed the name myoblastic myoma. Meyer believes that the tumors are derived, not from dedifferentiated or embryonal striped muscle, but from indifferent striped muscle that has lost to a large degree both the power of differentiation into striated muscle cells and the power of active proliferation. The congenital tumors and those occurring in situations where striped muscle is not normally present arise from misplaced muscle elements that become incapable of complete differentiation. The nodules arising in the tongue and in other situations where striped muscle occurs normally come from altered, previously differentiated striped muscle, which normally has only a limited regenerative capacity.

SCHLUTZ, Evanston, Ill. [ARCH. PATH.]

LYMPHOGRANULOMATOSIS OF BONE. E. UEHLINGER, Virchows Arch. f. path. Anat. **288**:36, 1933.

This report is based on the study of fifty cases of lymphogranulomatosis, in forty-eight of which the diagnosis was established by necropsy and in two by biopsy. The age of the patients varied from 12 to 77 years. Sixteen died in the third decade and twelve in the fourth. Twenty-three of the patients were males and twenty-seven females. Lymphogranulomatosis is a specific infection, which is histologically distinct from tuberculosis and lymphosarcoma. Primary involvement of bone or involvement limited to bone does not occur. Lymphogranulomatosis of the skeleton is a secondary process and arises either by direct continuity from a contiguous focus or by hematogenous metastasis. In Uehlinger's series, invasion of bone by direct continuity occurred twelve times and metastatic involvement five times. Under the metastatic cases Uehlinger includes only those in which the skeletal involvement was so widespread as to influence the clinical course of the disease. Direct erosive invasion occurred most often in the vertebrae, next often in the sternum and pelvis and least often in the ribs, clavicle and scapula. The process begins in the periosteum, penetrates the lacunae of the cortex and spreads in the marrow, which is pushed aside or replaced. In the gross the process cannot be distinguished from an invasive neoplasm. The roentgenologic picture is not characteristic. Invasion of bone is usually painless and generally occurs relatively later in the course of the disease. Invasion of bone by direct continuity led to no characteristic or striking changes in the blood in Uehlinger's cases. In the marrow histologically specific tissue is formed; this tissue quickly undergoes fibrosis, even in the absence of irradiation therapy. The bone undergoes osteolysis and osteoporosis. The formation of endosteal and periosteal bone was infrequent. The radiosensitivity of the tissue varied and appeared to depend on the duration of the disease as a whole. The distribution of the lesions in hematogenous skeletal involvement coincided with the distribution of red marrow in the adult. The process begins as specific osteomyelitis, which leads to replacement and fibrosis of the marrow. Clinically such cases were characterized by progressive anemia and leukopenia. The bone itself revealed relatively little change, and the roentgenologic findings were indefinite. The vertebrae, sternum and head of the femur were most often involved, the ribs, pelvis and cranium less often. Metastatic skeletal involvement occurred early in the course of the disease, which ran a rapidly progressive course.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

RENAL DWARFISM AND RENAL RICKETS. H. HAMPERL and K. WALLIS, Virchows Arch. f. path. Anat. **288**:119, 1933.

A detailed clinical and pathologic study of two cases of dwarfism is presented. Both patients were girls, aged 11 years and 3 months and 10 years and 5 months, respectively. The first had the stature of a girl of 6 years and 10 months, the second that of a girl of 5 years and 4 months. The body proportions were normal. The clinical findings were those of chronic interstitial nephritis, for whose onset no cause could be discerned in the history. The presence of chronic interstitial nephritis, with small contracted kidneys, was confirmed at necropsy. In the older girl, changes in the bones were very slight and were limited to the costochondral junctions of the ribs. The alterations were such as are seen in the ribs in very mild rickets. In the younger child, the roentgenologic and the histologic findings were those of marked rickets. The authors do not believe that the nephritis was the direct cause of either the dwarfism or the rickets. If any important rôle is to be ascribed to the nephritis, it seems necessary to assume that the renal factor acts on a special constitutional factor. The authors prefer to assume that the same noxa caused the nephritis, the infantilism and the rickets.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

TWO CASES OF CONGENITAL SACRAL TUMOR. W. MEISTER, Virchows Arch. f. path. Anat. **288**:286, 1933.

A tumor in an infant who died at the age of 3 days was situated anterior to the sacrum and coccyx and was not connected with the spinal cord or its membranes. It was cystic and consisted of derivatives of the three germ layers, tissue of central nervous system origin predominating. The tumor was a sacral teratoma, the origin of which is ascribed to incomplete separation of totipotent material from the gastrula. The second tumor, in a fetus of the eighth month, arose from the sacrum and coccyx and consisted of nonorganoid derivatives of the mesoderm. Its origin is ascribed to excessive growth of the mesoderm of the caudal end of the embryo beginning after gastrulation. SCHLUTZ, Evanston, Ill. [ARCH. PATH.]

HEALING STAGES OF PERIARTERITIS NODOSA AND THEIR RELATION TO JUVENILE ATHEROSCLEROSIS. E. JÄGER, Virchows Arch. f. path. Anat. **288**: 833, 1933.

Healed lesions of periarteritis nodosa are rarely seen, because the disease is usually a continuous and progressive process. In three men who died at the ages of 37, 30 and 39, the clinical duration of the illness was thirty-seven, fourteen and five months, respectively. In the first case a clinical diagnosis of periarteritis nodosa had been made early in the course of the disease. In each case necropsy revealed marked atherosclerosis. Microscopic study brought to light the changes in the small arteries which Jäger describes as the healed and healing lesions of periarteritis. In the case of shortest duration active lesions were also present. Injury to the media leads to hyperplasia of the overlying intima in the form of localized nodular thickenings. A single vessel may reveal several intimal nodules of different ages. Injury to the wall during the active stage may lead to the formation of miliary aneurysms; such aneurysms were seen especially in the coronary arteries. In the organization of thrombosed arteries, or aneurysms, blood channels are formed; about these there develop a new elastic membrane and a new media. The intimal hyperplasia bears no direct relation to lipoid infiltration, although the intimal nodules may sometimes be formed over what were originally superficial areas of lipoid infiltration. The formation of the intimal callus is not the result of atherosclerosis; when atheromatous degeneration occurs in the callus, it is the result of changes in the ground substance. Nodose atherosclerosis in younger persons, when associated with epicardial proliferation over the nodular areas of the coronary arteries and with scars of infarcts in the spleen and kidney, should suggest the possibility of healed periarteritis nodosa.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

BLOOD DYSCRASIAS AFTER INFECTION OF THE EAR, NOSE OR THROAT. W. KINDLER, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **24**:39 (March) 1933.

Kindler reviews an earlier observation of a case of acute myeloid leukemia which occurred immediately after a radical operation on the maxillary sinus in a previously healthy man. He also reports three new cases of dyscrasias of the blood occurring after infection of the otic or tonsillar regions. The first of these was a case of acute fatal leukemia following suppurative perichondritis of the auricle. The second case was one of a subacute leukemia with an aleukemic prodromal stage which followed nonspecific inflammation of the tonsils and cervical glands. The third case was one of purpura haemorrhagica with spontaneous, severe, late hemorrhage from the tonsillar abscess cavity, without any other manifest or latent signs of a hemorrhagic diathesis. A blood platelet count showed a severe thrombopenia as the cause of hemorrhage. An increase in the number of blood platelets and disappearance of hemorrhages followed injections of congo red. In the presence of a hemorrhagic diathesis acute and chronic infections of the tonsils play an important part in determining the occurrence and localization of hemorrhages in the pharyngopalatine region. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE COURSE AND PROGNOSIS OF PYLORIC STENOSIS WITH MEDICAL TREATMENT. N. FAXÉN, Acta pædiat. **14**:388 (April 28) 1933.

In 126 cases of pyloric stenosis in which the patients were treated without operation, the mortality was 5.5 per cent; this figure drops to 3.3 per cent if one excludes from the series three cases complicated by serious congenital malformations. The average duration of medical treatment in the hospital was seventy-five days, but was much longer in some cases, especially in those complicated by respiratory infections and in those in which artificial feeding was resorted to before the patient came under observation. If, during the first five or ten days of medical treatment, the patient's weight curve shows a rise, then the duration of required hospitalization may be forecast as relatively short, and vice versa. No description of the actual treatment is given except to emphasize the maintenance of fluid balance and the prophylaxis of infections, and to urge caution against excessively frequent lavage. The later prognosis relative to gastric symptoms in childhood and adult life, a point often emphasized by those who advocate surgical intervention, is not mentioned. The diagnostic criteria are perhaps open to criticism for their failure to include palpation of the tumor as a requisite.

McINTOSH, New York.

BILIRUBIN STUDIES IN CHILDHOOD. PAAVO HEINIÖ, Acta pædiat. **14**:453 (July 12) 1933.

The methods employed currently in the determination of bilirubin, including the van den Bergh test, are unsatisfactory. The author has found the method of Kerppola and Leikola much more to his liking. This procedure depends on the following facts: 1. Bilirubin, as found in bile and in the blood serum of so-called obstructive jaundice, is only slightly soluble in chloroform. 2. The type of bilirubin found in hemolytic icterus is readily soluble in chloroform. 3. Acidification of the first variety of bilirubin renders it soluble in chloroform. From these facts Kerppola and Leikola have concluded that bilirubin exists in two states, namely, so-called free bilirubin and soluble or "alkali" bilirubin. Free bilirubin is soluble in chloroform. It may be extracted from a chloroform solution by aqueous solvents the p_H of which is more alkaline than 5.5, although the extraction is not complete unless the p_H exceeds 11.0. At this p_H alkali salts of bilirubin are formed. When acid is added to such aqueous solutions until the p_H is lowered to 5.5, free bilirubin is formed and may be extracted with chloroform or with other lipoid solvents.

In the quantitative procedure, free bilirubin is dissolved directly in chloroform and is determined colorimetrically. Soluble or alkali bilirubin is acidified to convert it into the free state, then it is extracted with chloroform and quantified colorimetrically. Two modes of procedure are described for the latter determination. The standard is made of a 0.05 per cent solution of potassium bichromate, to which it is sometimes necessary to add a small quantity of cobalt nitrate in order to obtain an exact matching of colors. Duplicate readings on the same solution can be made with an accuracy involving a maximum error of 0.015 mg. of bilirubin per hundred cubic centimeters.

A total of 318 determinations of bilirubin were made on 130 subjects. In 143 duplicate determinations of total bilirubin, there was no difference between the two samples in 122; in 24 determinations there was a difference which averaged 0.72 per cent. In 143 determinations of free bilirubin, there was absolute agreement between the two samples in 119 cases, and in 21 cases there was a difference which averaged 0.72 per cent. Preliminary precipitation of the serum protein with alcohol gives lower values than other methods. As much as 66 per cent of the total serum bilirubin may be carried down with the protein precipitate, and it is very difficult to extract therefrom. This fact explains the greatest source of error in the van den Bergh method.

When applied to the serum of 26 normal infants within the first year of life, the Kerppola-Leikola method gave the following values: total bilirubin, 0.36 mg. per hundred cubic centimeters; free bilirubin, 0.16 mg.; soluble bilirubin, 0.20 mg. Free bilirubin averaged 44.4 per cent of the total bilirubin. Determinations were made on the serum of 27 children between the third and fourteenth years, with the following results: total bilirubin, 0.45 mg.; free bilirubin, 0.16 mg.; soluble bilirubin, 0.29 mg. Free bilirubin averaged 35.6 per cent of the total bilirubin. In 25 infants with icterus neonatorum the following values were obtained: total bilirubin, from 2.04 to 13.32 mg.; soluble bilirubin, from 0.40 to 2.52 mg.; free bilirubin, from 1.44 to 11.64 mg. The free bilirubin averaged 75.05 per cent of the total bilirubin. The diazo reaction was indirect. In 45 children with infectious jaundice (icterus catarrhalis) the following results were obtained: total bilirubin, from 0.69 to 4.38 mg.; free bilirubin, from 0.12 to 1.47 mg.; soluble bilirubin, from 0.54 to 2.91 mg. The free bilirubin averaged 24.1 per cent of the total bilirubin. In all of these cases the diazo reaction was direct.

Jaundice appears in cases of icterus catarrhalis when the serum bilirubin concentration is about 1 mg. per hundred cubic centimeters, whereas jaundice is not observed in icterus neonatorum until the serum bilirubin concentration is about 2 mg. In order to explain this fact, the author performed simultaneous determinations of the serum bilirubin and of the bilirubin in the fluid obtained from vesicles produced by the application of cantharidin to the skin. No explanation of the difference was arrived at. The concentration of bilirubin in the serum and that in the tissue fluids (vesicle fluid) were of the same order of magnitude and showed parallel variations. The concentration in the serum varied more rapidly than that in the tissue fluids.

The author discusses the findings in two cases showing combined hemolytic and obstructive jaundice.

McCune, New York.

A Micromethod for the Determination of the Sedimentation Rate. J. Ström, Acta pædiat. **14**:567 (July 12) 1933.

After some introductory remarks concerning the various technical factors entering into the determination of the erythrocyte sedimentation rate, the author describes a new microsedimentation procedure. He is careful to assert that this method is not so much a substitute for the standard macromethod of Westergren as a modification thereof, by virtue of which it may be performed with smaller quantities of blood. The author's tube is 200 mm. in length and 1 mm. in diameter. It is calibrated at distances of 25 mm., 100 mm. and 125 mm., respectively, from the tip. The following technic is employed. The pipet is filled to

the lowest mark (25 mm.) with 3.7 per cent sodium citrate. Blood is obtained by puncture of the ear or the finger-tip, and the tube filled to the mark farthest from the tip (125 mm.). The citrate and the blood are then ejected into a container, mixed and aspirated to the middle mark (100 mm.). As an alternative procedure, the citrate and the blood may be drawn separately into the tube to the marks at 25 and 100 mm., respectively, then ejected into a container and mixed.

Both the sensitivity of the method and the relationship between the values it gives and those obtained by Westergren's macromethod are subjected to statistical analysis. The material for this analysis comprises about 4,000 determinations, 1,134 of which were made in duplicate by the micromethod; 1,035 determinations were made simultaneously by both methods.

The author found that the two methods gave satisfactory agreement. Under 25 mm. the results were close, the microvalues being from 1 to 2 mm. higher than the macrovalues. Over 25 mm. the micromethod gave somewhat lower results. These agreements and variations are discussed and illustrated by charts and graphs.

McCUNE, New York.

HEREDITARY MULTIPLE EXOSTOSES. OLUF ANDERSEN, Acta pædiat. **14**:589 (July 12) 1933.

The author comments on the rarity of this entity and states that only forty families so affected had been reported up to 1931. To this number he adds two more. The first family includes a father and son. The second family includes twenty-seven members in four generations. Of this number, nine persons had the disease.

There are a brief description of the pathologic changes and the hereditary aspects and an enumeration and discussion of the possible etiologic factors.

McCUNE, New York.

INFECTIOUS MONONUCLEOSIS. F. WULFF, Ugesk. f. læger **95**:131 (Feb.) 1933.

Infectious mononucleosis is rather common. The severe form is often mistaken for diphtheria. The author thinks that administration of antitoxin (horse serum) is distinctly harmful. The blood picture is characteristic, and a blood film should always be examined before antitoxin is used in suspected cases.

ELGHAMMER, Chicago.

STOMATITIS. BEDRICH ZAK, Zubni lék. **32**:190 (July) 1932.

The etiology is cited as local defects and irritants, such as dust, tobacco and gas; tartar, poor oral hygiene and excessive heat or cold; intoxications, such as alcohol, mercury, lead, arsenic and iodine; infections such as scarlet fever, measles, grip, pneumonia or botulism, and general conditions, such as sunburn, diabetes and leukemia. The author presents a case of stomatitis mercurialis in a young female patient who had received intravenous injections of arsphenamine. Because of the severe pain in the base of the tongue, the question of a gumma was raised.

STULIK, Chicago.

Nervous Diseases

THE RELATIONS OF THE INTRACRANIAL PRESSURES. LEWIS H. WEED and LOUIS B. FLEXNER, Am. J. Physiol. **105**:266 (Aug.) 1933.

An experimental increase in the cerebrospinal pressure in the dog, brought about by the introduction of fluid into the subarachnoid space, results in a certain diminution of the intradural venous volume, but the pressure of the cerebral veins remains unaltered. Conversely, when the pressure of the cerebrospinal fluid is reduced mechanically or by tilting, the cerebral venous bed apparently compensates by dilatation, the venous walls expanding and permitting an increase in the

intradural venous volume, though maintaining the same pressure in the expanded channels. On the other hand, any change in the intracranial venous pressure results in a change in the cerebrospinal fluid pressure, about six tenths of the change in the venous pressure being effective in the fluid when the dislocation of the latter is minimal.

These findings indicate that the type of pressure equilibrium between the cerebral veins and the cerebrospinal fluid is that of an elastic membrane separating two fluids which are normally under almost identical pressures but which can exist under different pressures. The two fluids are, however, of unequal volume, that of the blood being far greater than that of the fluid. The venous blood is not necessarily confined within the cranium and is under direct or indirect vasomotor control; the cerebrospinal fluid is enclosed within fairly rigid membranes and cannot leave its craniovertebral container with any great rapidity.

NOURSE, Cleveland.

THE WATER OF THE CEREBROSPINAL FLUID; VARIATIONS OF ITS RATE OF FLOW WITH VARIATION OF VENTRICULAR PRESSURE. LOUIS B. FLEXNER, Am. J. Physiol. **106**:170 (Oct.) 1933.

Variations in the rate of production of cerebrospinal fluid with variations of intraventricular pressure have been studied. Within the range of ventricular pressure investigated the rate of formation of the water of the fluid appears to be a linear function of the difference between the effective hydrostatic pressure in the capillaries of the chorioid plexus and the hydrostatic pressure in the ventricles.

NOURSE, Cleveland.

A NOTE ON THE RATE OF CIRCULATION OF CEREBROSPINAL FLUID. LOUIS B. FLEXNER, Am. J. Physiol. **106**:201 (Oct.) 1933.

By using data on the rate of flow of cerebrospinal fluid from the aqueduct of Sylvius, on the volumes of the ventricles and on the volume of the subarachnoid space in adult cats, calculations were made of the rate at which new fluid replaces old in the different parts of the cerebrospinal fluid pathway. Within twenty-four hours it appears that fluid in the lateral ventricles is renewed seventeen times, in the third ventricle sixty times, in the fourth ventricle seventy-five times and in the subarachnoid space between four and five times.

NOURSE, Cleveland.

THE INFLUENCE OF EMOTIONS IN PRECIPITATING CONVULSIONS. S. BERNARD WORTIS, Am. J. Psychiat. **13**:725 (Jan.) 1934.

Emotion is now a well recognized immediate cause of some convulsions. This study represents three and one-half years' investigation of forty-two unselected cases to determine how frequently emotions precipitate a convulsion. In thirty-one of these cases there was a direct relationship between emotions and one or more of the major convulsions. In several instances all, or nearly all, attacks were immediately preceded by a strong feeling of fear, guilt or frustration. In eight patients attacks were precipitated under observation by discussion of the particular emotional difficulty in question. In three patients attacks could be precipitated at will by the physician by such discussion. Many of the patients in whom the emotions served as a precipitating factor had definite organic disease of the brain. One had a tumor of the brain, while in others the history or examination showed evidence of injury at birth or other cerebral trauma.

The emotional factor is explained on the basis of stimulation of the sympathetic nervous system.

JAHR, Omaha.

RESPIRATORY METABOLISM OF EXCISED BRAIN TISSUE; THE RESPIRATORY QUOTIENT. S. BERNARD WORTIS, Am. J. Psychiat. **13**:726 (Jan.) 1934.

The experimental work described was done on a rat's brain obtained after sudden decerebration of the animal without anesthesia. The rate of oxidation of the different foodstuffs was studied by accepted biochemical determinations, whereby the respiratory quotient was deduced. The results are confirmatory of previously

recorded data showing that the different kinds of tissue composing the central nervous system have different rates of consumption of oxygen. Thus, the gray matter uses more oxygen than the white matter or the spinal nerves. The addition of dextrose to the immersion fluid (Ringer's solution) enhances the intake of oxygen. This action depends on the resultant lactic acid from the dextrose. The lactic acid content of the brain depends directly on the blood sugar level. The rôle of particular foodstuffs in the convulsive phenomena is not definite. Cat brain obtained after convulsions caused by camphormonobromide showed no peculiarity in the uptake of oxygen.

JAHR, Omaha.

THE EFFECT OF INTERCURRENT CHRONIC PULMONARY TUBERCULOSIS ON THE CONVULSION THRESHOLD IN EPILEPSY; A STUDY OF 100 CASES. I. J. KARLSBERG, Am. J. Psychiat. **13**:799 (Jan.) 1934.

Thirty-nine males and sixty-one females suffering from clinically active pulmonary tuberculosis and epilepsy were studied from the standpoint of the monthly average rate of convulsions prior to the onset of tuberculosis, and this rate was compared with the average monthly rate of seizures during the period of tuberculous activity. There was a general decline in the number of seizures when the patients were ill, the greatest decline corresponding to the intensity of the tuberculous process and its clinical course (fever, emaciation, etc.). In those who recovered from their tuberculosis the former rate of seizures returned when the clinical symptoms subsided.

An attempt is made to explain the phenomenon on biochemical equilibration, since tuberculosis is characterized by findings opposite to those of epilepsy. Thus,

Tuberculosis	Epilepsy
Basal metabolic rate increased	Basal metabolic rate decreased
Blood calcium elevated	Blood calcium normal or decreased
Blood chlorides usually low	Blood chlorides elevated
Hyperglycemia frequent	Low blood sugar, frequently associated with convulsions
p_H tendency to the acid side	p_H tendency to alkaline side

JAHR, Omaha.

RELATION OF PREMATURE BIRTH AND UNDERWEIGHT CONDITION AT BIRTH TO MENTAL DEFICIENCY. AARON J. ROSANOFF and CHRISTINE V. INMAN-KANE, Am. J. Psychiat. **13**:829 (Jan.) 1934.

Various groups of premature and immature children were studied from the point of view of mental deficiency. The questions specifically to be determined were: (*a*) How does the incidence of premature birth (three weeks or more before term) and of underweight condition at birth (less than 5½ pounds [2,494.8 Gm.]) among the feebleminded compare with that in the unselected population? (*b*) How does the incidence of mental deficiency among those prematurely born, those who were underweight at birth and those who were both prematurely born and underweight at birth compare with the incidence in the unselected population?

Among 122 patients with mental deficiency in institutions, 21.3 per cent had been born prematurely and were immature. The corresponding percentage for the controls was 3.89. Among 146 children of elementary school age who had been born prematurely or who were immature, there were 15 cases (10.27 per cent) of mental deficiency. An unselected control group showed 2.63 per cent.

A comprehensive review of the literature is included.

JAHR, Omaha.

THE MENTAL HYGIENE PROBLEMS OF THE DEAF. IRA S. WILE, Arch. Pediat. **50**:603 (Sept.) 1933.

This article is a discussion of the problems of mental hygiene peculiar to the deaf. Too infrequently the deaf are regarded as persons who lack hearing, with the emphasis on the aural inadequacy. They should be regarded as persons who

are not integrated in the same biologic level as those who hear, because of an auditory block. Deaf persons are handicapped in the growth of personality by reason of deficiency factors in ideation. The intelligence of the deaf is measured with difficulty, and ordinary intelligence tests often suggest mental inadequacy which is not in harmony with the facts. Wile doubts that mental deficiency is much more frequent among the deaf than among those who hear, and believes that there is a need for better methods of testing the mentality of deaf persons.

Various mental tests of the deaf are discussed and suggestions for a better handling and a better understanding of such persons advanced.

WADDELL JR., University, Va.

MATERNAL RESPONSIBILITY IN MICROCEPHALY. ELLSWORTH MOODY, Arch. Pediat. **50**:658 (Sept.) 1933.

The histories of two families are presented which strongly suggest that the female germ plasm may be definitely responsible for the microcephalus.

WADDELL JR., University, Va.

THE NEUROLOGIC ASPECT OF SOME INVOLUNTARY RESPONSES TO AFFECTIVE AND RELATED PHENOMENA OF INFANCY AND CHILDHOOD. SAMUEL M. WEINGROW, Arch. Pediat. **50**:677 (Oct.) 1933.

The automatic, voluntary and associative systems of the normal infant and child are outlined, and pathologic cases showing abnormal reactions of the automatic system are described.

This article does not lend itself to satisfactory abstracting.

WADDELL JR., University, Va.

ANTHROPOMETRIC AND ANTHROPOSCOPIC STUDIES OF POLIOMYELITIS. H. E. THELANDER and HELEN B. PRYOR, Arch. Pediat. **50**:749 (Nov.) 1933.

One hundred patients paralyzed as a result of poliomyelitis were compared with 518 normal controls in an effort to determine variations in anthropometric measurements when compared by age and sex, except those readily explained as a result of the disease. Morphologic characteristics compared by observational methods showed no consistent outstanding difference between those who had had poliomyelitis and the control groups, with the possible exception of a predominance of a high narrow palate in the children who had had poliomyelitis. In those with extensive atrophy of the muscle and bone due to paralysis, no difference in subcutaneous tissue could be demonstrated between the paralyzed limb and its nonparalyzed mate.

WADDELL JR., University, Va.

EPIDEMIC CEREBROSPINAL FEVER IN CHILDHOOD. E. B. SHAW and H. E. THELANDER, J. A. M. A. **101**:746 (Sept. 2) 1933.

A series of fifty-eight consecutive cases of cerebrospinal fever occurring over a period of ten years is reported. The group presented unusual prominence of signs of systemic invasion evidenced by signs of general intoxication and the presence of a diffuse purpuric eruption. The latter was present in 62 per cent and was of great diagnostic value. Its presence in obscure, severe febrile illnesses is highly suggestive. This series further illustrates the statement that meningitic symptoms do not always predominate. It is thought that vascular damage produced by meningococcic toxins is responsible for the eruption and many of the manifestations of infection, and permits the characteristic invasion of the blood stream. Treatment should be based on the recognition of signs other than those of meningitis. It must be designed to combat intoxication by intravenous administration of serum followed by intraspinal injections. BONAR, Salt Lake City.

ACUTE TRANSITORY CEREBRAL MANIFESTATIONS IN INFANTS AND IN CHILDREN. A. LEVINSON, J. A. M. A. **101**:765 (Sept. 2) 1933.

Acute transitory cerebral manifestations appear suddenly usually during the autumn and winter with high fever, apathy or convulsions. The child is comatose or drowsy, his neck is rigid and the Brudzinski and Kernig signs are positive. The physical examination may disclose no other conditions, or there may be a red throat, congested ear drums or an occasional râle. The manifestations last for a day or two and subside, and the diagnosis is established by finding some condition such as otitis media, pneumonia, pyelitis, infection of the upper respiratory tract or rheumatic fever. In some cases no underlying cause can be found. The important question is differentiation from epidemic meningitis. The cerebrospinal fluid is increased in amount and pressure; the cells are normal, and the sugar content is increased. A normal cell count indicates no meningeal reaction; an increased count, some reaction. A normal or even high sugar, however, does not rule out meningitis. A rapid respiratory rate is not usually found in meningitis. The presence of petechiae indicates meningococcemia. When no clinical diagnosis can be made, spinal puncture may be resorted to safely. Treatment cannot be generalized. In some cases no treatment is necessary. In others intramuscular injections of 10 per cent solution of magnesium sulphate is of value in relieving convulsions.

BONAR, Salt Lake City.

THE NATURE OF EMOTION. WILLIAM MCDOUGALL, J. Abnorm. Psychol. **28**:245 (Oct.-Dec.) 1933.

McDougall defends his concept that each primary emotional quality is an aspect of the working of one of the instincts. In any state of primary emotional or instinctive excitement the fact of experience and the fact of outward activity are two aspects of one and the same concrete series of events. The conative (affective) experience is also an essential part, feature or aspect of the emotional experience. Distinction should be made between structure and function, between a disposition and the activity arising in the excitement of that disposition. The term instinct should be reserved for the innate disposition to some mode of behavior common to the species, some other expression being employed for the actual process or activity in which the disposition manifests itself. Instinctive activity is always accompanied by symptoms or signs of emotion, its distinctive mark being the impulse, urge or drive toward a goal. Even simple instinctive activities, e. g., sneezing, coughing, scratching, are not entirely devoid of emotional quality. Every form of instinctive striving may oscillate between the two poles of satisfaction, or pleasure, and dissatisfaction, or pain. Distinction must be made between true emotional qualities and the "derived emotions," or complex feelings.

ABRAMSON, New York.

CLINICAL PATHOLOGY OF EPIDEMIC ENCEPHALITIS. GEORGE IVES, J. Missouri M. A. **30**:431 (Nov.) 1933.

The clinical changes in the St. Louis type of epidemic encephalitis were found almost entirely in the blood and spinal fluid. In almost every case both the blood and spinal fluid showed pathologic variations. The variations found in these fluids were not pathognomonic of encephalitis, yet were of great value. Without these findings the diagnosis must be incomplete. The Schilling differential count was of little value in diagnosis; the prognosis could not be based on findings in the blood or spinal fluid, and no etiologic agent was found in either the blood or the spinal fluid. Leukocytosis occurred in 82.9 per cent of the cases. The spinal fluid was always abnormal. Lymphocystosis was usual, with a moderate increase in globulin. Pellicle formation was noted in a few instances. The pressure was usually increased.

Forty-one cases were observed. The blood was studied in thirty-five cases, and the spinal fluid in thirty-nine.

BERGER, Kansas City, Mo.

NEUROLOGICAL MANIFESTATIONS OF EPIDEMIC ENCEPHALITIS; A PRELIMINARY REPORT ON THE ST. LOUIS 1933 EPIDEMIC. JAMES F. MCFADDEN, J. Missouri M. A. **31**:96 (March) 1934.

While numerous structures of the body are involved in encephalitis, the nervous system bears the brunt of the attack. It is here, therefore, that one would expect to find most of the evidence of the ravages of the disease.

At postmortem examination of patients with this disease multiple hemorrhages were seen in the walls of the blood vessels in the nerve structure. For this reason one must conclude that some of the damage done is permanent. The organic changes are accompanied by psychiatric manifestations, which are found in other organic diseases of the brain, and by cranial nerve dysfunctions, such as tremor, disturbed reflexes and disorders of gait and station, as well as by various sensory nerve disturbances.

Of fifty patients admitted to the Des Loge Hospital of St. Louis University, 60 per cent showed inequality of the pupils; 30 per cent still showed this change at the time of discharge. Photophobia was present in 10 per cent, strabismus in 4 per cent and nystagmus in 18 per cent.

Inequality in the palpebral fissures and unequal innervation of the tongue or one side of the face were present in 52 per cent. Toe reflexes were present in 54 per cent and were distributed as follows: Babinski's sign, on admission in sixteen patients and at discharge in five; Chaddock's sign, on admission in seven and at discharge in one; Gordon's sign, on admission in five and at discharge in five, and Oppenheim's sign, on admission in twenty-one and at discharge in three. Rigidity of the neck was present on admission in 82 per cent and Kernig's sign in 40 per cent. Patellar and ankle clonus were present in one case both on admission and at discharge and present in three others at the time of discharge.

"Tremors, fine, coarse or rhythmical, were present in a very large number of outgoing cases. These tremors were of the lower facial muscles, tongue, eye lids, extremities or of the entire body."

An increased number of cells were present in the spinal fluid in 96 per cent of the cases.

During the early stages of the disease the signs noted were not constant, but often varied from day to day.

BERGER, Kansas City, Mo.

RELATION BETWEEN NUTRITION, MENTAL LEVEL AND ADJUSTMENT IN DELINQUENT BOYS. MATTHEW MOLITCH and AUGUST K. ECCLES, J. Nerv. & Ment. Dis. **78**:123 (Aug.) 1933.

No positive relationship has been found to exist between good nutrition and behavior. By a new anthropometric technic the authors have undertaken a study of all the inmates of the New Jersey State Home for Boys at Jamesburg. Many children whom Molitch regarded as underweight were found to be average or above average weight when the width of their skeletal framework was taken into consideration. Negroes were found as a class to have narrow skeletal width, while Poles and Italians had a wide frame. The American white natives range between these two groups. Psychometric measurements were made with the Stanford-Binet, Kuhlman-Anderson, Morgan, Healy picture completion, Porteus maze and other tests.

Eight hundred boys, aged between 8 and 18, were studied according to the racial width-height index. From the psychologic standpoint a study of 554 cases revealed no significant difference in general mental level or in overt behavior between those who were well nourished and those who were undernourished. However, the undernourished group exhibited a shade of disadvantage in both mentality and quality of social adjustment. The writers thus substantiate the findings of Healy that the delinquent boy is not the undernourished boy.

HART, Greenwich, Conn. [ARCH. NEUROL. & PSYCHIAT.]

ACUTE ASCENDING MYELITIS FOLLOWING THE ADMINISTRATION OF TYPHOID VACCINE. R. FINLEY GAYLE and RICHARD A. BOWEN, J. Nerv. & Ment. Dis. **78**:221 (Sept.) 1933.

An 18 year old boy was given an injection of 0.5 cc. of typhoid-paratyphoid vaccine furnished by the Army Medical School for use in the National Guard. After a few days the patient complained of numbness of the arms and legs and fatigue. There was no muscular weakness. A second dose of 0.5 cc. of vaccine was administered thirteen days after the first dose. Subsequent to this injection diffuse muscular weakness developed, involving the legs and, to a lesser extent, the arms, and gradually going into flaccid paralysis. There was no cranial nerve palsy. The knee, elbow and ankle jerks were absent, and there was no abdominal reflex. There were dysphagia and a fine lateral nystagmus. The spinal fluid pressure was normal. The fluid showed 3 cells per cubic millimeter; 68 mg. of sugar, and 618 mg. of chlorides per hundred cubic centimeters. The Wassermann and colloidal gold reactions were negative. The urine was normal. The white blood cells numbered 15,700, with 88 per cent polymorphonuclear cells. The nonprotein nitrogen was 50 mg. per hundred cubic centimeters. The patient died of a bulbar condition forty-four days following the first injection.

Postmortem examination showed no pathologic changes in the dura or arachnoid. There was some congestion in the cerebrum, cerebellum, pons, medulla and upper part of the spinal cord. The peripheral nerves were moderately swollen and congested. On microscopic examination the vessels in the several portions of the nervous system were seen to be dilated, but there was no alteration in their walls. The motor cells in the anterior horn of the cord and nuclei in the medulla were swollen and irregular in outline, with chromatolysis and granular disintegration. The pathologic report ended thus: "It is impossible to make a diagnosis from the morbid anatomy. The subject did not have poliomyelitis or encephalitis lethargica. He did have polyneuritis with definite cellular changes in the motor portion of the cord and medulla. When the symptoms of the condition are considered with the pathologic changes, the most likely diagnosis is Landry's paralysis."

A review of the literature is submitted.

JAHR, Omaha.

PROGRESSIVE BULBAR PARALYSIS. MAX HELFAND, J. Nerv. & Ment. Dis. **78**:362 (Oct.) 1933.

Helfand has searched the literature from 1910 to the present for an account of what was defined by Charcot, Duchenne and Oppenheim as progressive bulbar paralysis and has not found one of this syndrome uncomplicated by other symptoms and verified pathologically. Bulbar syndromes occur, of course, as in poliomyelitis, arteriosclerosis, syphilis, tumors, vascular insults, multiple sclerosis and other conditions. Helfand reports the clinical and pathologic details in four cases which add doubt as to the existence of a disease entity called progressive bulbar paralysis, and he considers that the disease which has been described is merely a generalized morbid process of amyotrophic lateral sclerosis with a bulbar syndrome. In three of his four cases there were unmistakable findings of the latter disease, while only one case might be called true progressive bulbar paralysis, as it was unaccompanied by degeneration of the pyramidal tract. In the spinal cord the cells of the anterior horn are chiefly diseased while those in the lateral horn are more or less normal. The various nuclei of the medulla are involved in degenerative changes without any evidence of functional or phylogenetic predilection for amyotrophic lateral sclerosis; the cells of the spinal cord are chiefly involved, but an irregularity of localization should not serve as sufficient evidence to cause doubt as to the identity of one disease process in various cases. Almost every disseminated disease has localizable types without severing each from the main group. Cerebrospinal syphilis, multiple sclerosis and encephalitis pontis are cases in point. In amyotrophic lateral sclerosis the affinity of the toxin is less for mesodermal tissues than for the plasma of the nerve cell. Helfand concludes, therefore, that progressive bulbar paralysis is a syndrome of other disease entities, mostly of amyotrophic lateral sclerosis, in which the constellation of causative factors,

including the process of senility, is most likely precipitated by an exogenic toxin which influences neural as well as mesodermal tissue.

HART, Greenwich, Conn. [ARCH. NEUROL. & PSYCHIAT.]

ENCEPHALOGRAPHIC STUDIES IN CHILDREN. BERNARD S. BRODY and PAUL F. MCALENNEY, J. Pediat. **4**:159 (Feb.) 1934.

The encephalographic findings in eight selected cases are discussed. In four cases of microcephalic idiocy symmetrically enlarged ventricles were considered as characteristic of this condition. Encephalography is considered to be of great value in the selection of epileptic children who may be benefited by surgical intervention. In two instances of porencephalia the convulsive seizures stopped after an injection of air. The technic used in encephalography is discussed in detail.

LEMASTER, Evanston, Ill.

RECOVERY FROM INFLUENZAL MENINGITIS. D. H. DUNCAN and C. H. WEBB, J. Pediat. **4**:216 (Feb.) 1934.

An 8 year old boy with acute meningitis due to Pfeiffer's bacillus recovered completely. The essential treatment consisted of removal of cerebrospinal fluid by lumbar puncture either daily or twice daily. The literature contains reports of recovery from influenzal meningitis in only twenty-seven other cases.

LEMASTER, Evanston, Ill.

TETANY OF THE NEWBORN. JOHN DORSEY CRAIG, J. Pediat. **4**:219 (Feb.) 1934.

A new-born boy began to have convulsions on the ninth day of life. The convulsions were frequent. On the fifteenth day of life chemical analysis of the blood showed 7.3 mg. of calcium and 4.4 mg. of phosphorus per hundred cubic centimeters of blood. The convulsions stopped immediately after calcium gluconate, calcium chloride and cod liver oil were given. Recovery and subsequent growth were uneventful.

LEMASTER, Evanston, Ill.

THE NIRVANOL TREATMENT OF CHOREA. S. W. MARICK, J. Pediat. **4**:242 (Feb.) 1934.

Excellent results were obtained in the treatment of more than sixty children suffering from chorea with phenylethylhydantoin. The author believes that it is unnecessary to hospitalize patients receiving this treatment. Phenylethylhydantoin is preferred to injections of typhoid vaccine because it is safer and does not cause shock. From 5 to 15 grains (0.3 to 0.97 Gm.) of the drug was used daily. The best results were obtained in moderately severe and severe cases of chorea, but recurrences were not prevented.

LEMASTER, Evanston, Ill.

MALADAPTATION AS A FACTOR IN THE ETIOLOGY OF NEUROSIS. W. W. BARBER, J. Pediat. **4**:304 (May) 1934.

The factors influencing the maladaptation of neurotic children are discussed. The environment in the home, rather than heredity, is considered to be the chief cause. Faulty management by the parents causes the child to be restless, irritable and maladjusted. Prevention and treatment depend solely on good management and a clear understanding of the nature of the process.

LEMASTER, Evanston, Ill.

ACUTE MENINGITIS DUE TO BACILLUS FECALIS ALCALIGENES. ROBERT J. MASON, J. Pediat. **4**:514 (April) 1934.

A case of acute meningitis due to Bacillus faecalis-alcaligenes in a 12 year old girl is reported. The source of infection was considered to be by way of a lumbo-

sacral meningocele. Recovery followed repeated drainage of cerebrospinal fluid by cisternal punctures. Although the organism is usually harmless, undoubtedly it becomes pathogenic at times.

LEMASTER, Evanston, Ill.

BULBAR POLIOMYELITIS AND ITS TREATMENT. EMIL SMITH and HENRY I. FINEBERG, J. Pediat. **4**:590 (May) 1934.

The clinical picture of unilateral and bilateral paralysis of the soft palate in the bulbar type of poliomyelitis is discussed. The suggested treatment consists essentially of postural drainage with the head low, the aspiration of secretions from the throat and the administration of fluids by rectum and by hypodermoclysis. Lumbar puncture is not advised. The use of the respirator is definitely contraindicated. Drugs are of little or no value. Nasal gavage is not begun until the fever has subsided.

LEMASTER, Evanston, Ill.

THE RÔLE OF CHILD GUIDANCE IN THE PREVENTION OF SCHIZOPHRENIA (DEMENTIA PRAECOX). H. L. LEVIN, New York State J. Med. **33**:805 (July 1) 1933.

Schizophrenia, which incapacitates more persons in this country than does cancer or tuberculosis, may be warded off if early "warning signs of impending disaster" are detected in children and if the child is then put in a child guidance clinic. Cases are reported to show how the "inadequate type of child," the "precocious type," the neurotic type, the day dreamer and the child who never grows up emotionally may be handled to prevent the development of dementia praecox.

Both the public and the medical profession must be taught to detect the early signs of mental disease in childhood.

AIKMAN, Rochester, N. Y.

SOME RELATIONSHIPS BETWEEN PERSONALITY AND BODY CHEMISTRY. GILBERT J. RICH, J. Neurol. & Psychopath. **14**:132 (Oct.) 1933.

A discussion of the relationship between acid-base balance and total behavior is presented. There is a definite positive correlation between emotional excitability and relative alkalinity of the saliva. The excitable person tends to have a less acid saliva than does the calm and apathetic person. The same is true of the urinary acidity. In gross personality deviations of mental disease there is a disturbance of the acid-base balance and, by and large, lowered acidity tends to be associated with the more active states and heightened acidity with the more apathetic conditions. An effort is made to explain these phenomena on the basis of the respiratory factors regulating the formation and elimination of carbon dioxide.

Creatinine, an important body metabolite, is also discussed from the standpoint of personality characteristics. The most excitable persons tend to have both the lowest concentration of creatinine in the blood and the smallest relative amounts of creatinine in the urine. The author raises the question: Should one speak of personality, considered as the gross pattern of behavior, as dependent on the condition of the neuromuscular system rather than that of the nervous system, or must one consider the relationship as due to the action of creatinine as a drug which modifies behavior?

The results of studies on phosphorus and calcium were too conflicting to permit the drawing of plausible conclusions.

JAHR, Omaha.

HEREDITY AND PSYCHIATRY. J. Neurol. & Psychopath. **14**:139 (Oct.) 1933.

Editorial comment is made on the inadequate correlation between eugenics, the study of heredity and the study of disease, especially that pertaining to psychiatric conditions. A plea is made for further study of the neglected science of heredity as related to familial tendencies to certain diseases and reactions to toxins and drugs and particularly to familial tendencies and responses to environmental stimuli.

JAHR, Omaha.

TWO CASES OF AMYOTONIA CONGENITA (WERDNIG-HOFFMANN'S DISEASE). HELEN MACKAY, Proc. Roy. Soc. Med. **27**:120 (Dec.) 1933.

The first case reported is that of a girl, aged 2½ years. She was one of five children, two of whom were healthy. Two had died of pneumonia and the other of amyotonia congenita. The second case is that of a girl, aged 1¾ years. The mother had had three pregnancies; the first child died in the hospital when nearly 2 years old, from general weakness; the second child was stillborn. The Wassermann reaction of the mother was negative. WILLIAMSON, New Orleans.

SPONTANEOUS MENINGEAL HEMORRHAGE WITH TRANSITORY HEMIPLEGIA. J. M. MACERA, J. P. KÄFER and M. F. VAQUER, Arch. argent. de pediat. **4**:351 (May) 1933.

The authors report this very rare condition in a child 13 years old.

Simultaneously with the meningeal hemorrhage, the child showed multiple hemorrhages in the conjunctivae, the kidneys and the retinas and from the nose. The blood platelets were normal, as were the bleeding and clotting time. Clinically, there were numerous signs of meningeal involvement, such as rigidity of the neck, a positive Kernig sign and some limitation of motion in the extremities. There was also facial paralysis on the left. The Wassermann and Kahn reactions were definitely positive.

The authors believe that the causative factor was syphilis.

SCHLUTZ, Chicago.

SCHILDER'S DISEASE. J. M. VALDÉS and C. PIANTONI, Arch. argent. de pediat. **4**:566 (Aug.) 1933.

The authors report this rare disorder in three boys of the same family. The ages ranged from 6 to 11 years. On the maternal side, there were alcoholism and various grave nervous disorders.

All the patients had the typical symptoms, consisting of sensory disturbances, spastic paralyses, serious mental involvement and a progressive course. One case ended fatally. The observations at autopsy showed the lesions typical for this disorder.

SCHLUTZ, Chicago.

THE TREATMENT OF CHOREA WITH NIRVANOL. LEON VELASCO BLANCO and HECTOR ABRINES, Arch. argent. de pediat. **4**:884 (Dec.) 1933.

The authors report successful treatment with phenylethylhydantoin in three cases. They conclude that the optimal effect is obtained if treatment is begun early. The rash appeared in all three cases, but the authors are of the opinion that the appearance of the rash is not necessary in order to indicate benefit from the use of the drug. They prefer the use of one large dose daily—0.3 Gm.—rather than fractional doses given several times a day.

The rash caused by this drug has a different distribution from the measles rash in that it usually appears first on the extremities and finally invades the head. The eruption often appears symmetrically, especially on the extremities.

No arthropathy, urinary disturbance or glandular enlargement was noticed in the authors' cases. There was no itching, and the eruption was not followed by desquamation.

SCHLUTZ, Chicago.

A CASE OF CEREBROSPINAL MENINGITIS. O. DA VEIGA, Arch. de pediat., Rio de Janeiro **7**:634 (March) 1934.

In the case reported in this article the patient recovered after the injection of 80 cc. of antimeningococcic serum given cisternally. SANFORD, Chicago.

PREPUBERAL TETANY. LUIS MORQUIO, Arch. de pediat. d. Uruguay **4**:384 (Sept.) 1933.

This rare condition occurred in a girl about 12 years old. Almost continuous tetany, affecting all the extremities, had lasted for more than a year and had resulted in actual contractures. The Trousseau, Erb-Westphal and Chvostek phenomena were pronounced. The basal metabolic rate was 17 per cent above normal. There was definite hypocalcemia. The alkaline reserve was normal. Ultraviolet irradiation and the liberal use of calcium salts caused marked improvement in the condition.

SCHLUTZ, Chicago.

SPASMOPHILIA. G. VIDAL JORDANA, Paidoterapia **12**:537 (Oct.) 1933.

Since the time that Themich gave the name to the entity spasmophilia and Finkelstein wrote his monograph on the subject, many ideas have been added, some of them leading to further explanations, others only complicating the picture. Three fundamental, classic findings are necessary for diagnosis: mechanical hyperexcitability, electric hyperexcitability and hypocalcemia. Though spasmophilia belongs to the group of neuropathic diatheses, with incomplete symptomatology the diagnosis should be paraspasmophilia.

The theory that spasmophilia is due to a sensitization to protein from the digestive tract is wrong. Parathyroid insufficiency, on the other hand, is an important etiologic factor, though it is not the only one. With parathyroid extract a rapid cure has been obtained in fourteen cases. Hypocalcemia is always present, and there is a definite relation between the normal amount of neuromuscular contractility and the equilibrium between the monovalent sodiopotassium and bivalent calciomagnesium ions. There is a reduction of the ionized calcium; but it is a question as to whether this reduction is due to the alkalosis or to the diminution of the total amount of calcium.

There are few new facts in regard to the symptomatology. Fever is of doubtful significance, and also Chvostek's sign, and chronaxia is of much less value than the routine use of the galvanic current for hyperexcitability.

From the standpoint of therapeutics, parathyroid extract has been preferred recently, but any known remedy which tends to increase the amount of ionized calcium of the blood is applicable.

HERRON, Spokane, Wash.

HYSTERIA IN A CHILD. JULIAN T. RUBIO GARCIA, Pediatría españ. **22**:571 (Sept.) 1933.

This comparatively rare condition in childhood occurred in a child aged 5 years and manifested itself chiefly in wilful vomiting. Parasitic infestation with Tricocephalus was a complicating feature. Various forms of treatment are discussed. The most successful is a combination of psychic and physical treatment and a sensible educational approach.

SCHLUTZ, Chicago.

Diseases of the Eye

TREATMENT OF STRABISMUS IN CHILDREN BY THE FAMILY PHYSICIAN. J. A. and LIONEL DARCHE, Union méd. du Canada **43**:76 (Jan.) 1934.

The authors plead for earlier treatment of strabismus by the family physician, who can see the child in the preschool years. If the condition is allowed to go on until the child is 8 or 10 years old, vision in the weaker eye will be first suppressed, then lost altogether. Treatment consists in forcing the weak eye to undertake vision, either by blindfolding the good eye or by keeping it dilated with a 1 per cent solution of atropine. Glasses should be fitted and worn constantly as soon as possible. With the simple treatment outlined, fusion of images is once more made possible, and binocular vision regained.

DAFFINEE, Boston.

HAMARTOMA OF THE LACRIMAL CARUNCLE. S. SGROSSO, Arch. di ottal. **41**:90 (Jan.-Feb.) 1934.

An infant with a mass the size of a large pea in the inner angle of the eye was seen. The globe was microphthalmic, with a cataractous lens. The mass arising from the caruncle was adherent to the sclera. It was removed without injuring the globe, and the inner angle was reconstructed with the remaining skin and conjunctiva. The tumor measured 17 by 12 mm. It contained fatty tissue with some glandular tissue. Since the elements present showed the characteristics of normal tissue the tumor is classed as a hamartoma (Albrecht) and not as a blastoma. Its presence in fetal life had apparently interfered with the normal development of the globe.

GIFFORD, Chicago. [ARCH. OPHTH.]

A CASE OF BILATERAL CONGENITAL HYDROPHTHALMOS, ACROCEPHALOSYNDACTYLIA AND OTHER MALFORMATIONS. P. J. WAARDENBERG, Klin. Monatsbl. f. Augenh. **92**:29 (Jan.) 1934.

The detailed report of an unusual combination of congenital malformations is given and illustrated with nine photographs. A baby born at full term, weighing 2,770 Gm. and measuring 50 cm., the child of nonrelated parents, died with symptoms of cyanosis on the fourth day after birth. Hydrophthalmos of both eyes was noted, as well as ocular hypertelorism, the distance between the inner canthi measuring 32 mm., against a normal average of 22 mm. The corneas were opaque, and the limbus was ill demarcated from the sclera. Other malformations were acrocephalosyndactylia, "parrot's nose," cleft palate, badly developed mandibles and chin, low-set and malformed ears, malposition of the clavicles, mitral stenosis, pseudohermaphroditism, cryptorchism and contraction of the elbow and knee joints.

Roentgenograms showed irregularities of the skull, hands and feet.

The case is discussed in comparison with other instances recorded in the literature, and especially in connection with the zoologic publication of Bonnevies, which seems to be supported in some respects by Waardenberg's case. Etiologic consideration is given the increased intracranial pressure which was present though the cranial sutures were open and the fontanels patulous.

STOLL, Cincinnati. [ARCH. OPHTH.]

A CASE OF SEVERE OCULAR SCROFULOSIS. W. STOCK, Klin. Monatsbl. f. Augenh. **92**:117 (Jan.) 1934.

Very large phlyctenules recurred over and over again in both eyes of a girl aged 15. They involved nearly the entire conjunctiva bulbi, formed necrotic areas and left considerable scars. The cornea of the right eye was almost entirely scarred by large infiltrations and ulcers, reducing vision to mere perception of light. Owing to similar processes the vision of the left eye was reduced to 0.1/60. After all other treatments failed, transfusion of 150 cc. of the mother's blood was resorted to. On the following day the eyes were less congested. No relapse occurred; complete recovery was obtained; the corneas cleared, and vision rose to 5/60. In the author's opinion, certain blindness was prevented by the transfusion.

STOLL, Cincinnati. [ARCH. OPHTH.]

A CASE OF CONGENITAL OPHTHALMOS. JOHANN VON PETHEÖ, Monatschr. f. Kinderh. **59**:254, 1934.

An 8 day old infant was born with total absence of the eyes. The sockets were intact and were lined with a hard membrane. There was no trace of eyebrows or eyelashes. Fortunately the child died of pneumonia.

GERSTLEY, Chicago.

PREVENTION OF HEREDITARY CONDITIONS OF THE EYE. B. FLEISCHER-ERLANGER, München. med. Wchnschr. **81**:17 (Jan. 5) 1934.

Fleischer-Erlanger tells of his previous investigations of this subject, which has become of more acute importance because of the question of sterilization of

persons whose descendants may have transmitted to them one of many such defects of the eye.

The mendelian theory is used as a basis, and the literature of the past, with its stastistics as to hereditary conditions of the eye, is dwelt on in detail. The author adds the following classification of the various conditions of the eye as to hereditary possibilities:

	Recessive	Dominant	Dominant but Irregular	Recessive Sex-Linked
Retina				
	Retinitis pigmentosa	Certain forms of retinitis pigmentosa	Some macular degenerations	One form of retinitis pigmentosa
	Degeneration of macula lutea	One form of detachment	Lindau's disease	One form of macular degeneration
	Aplasia maculae with nystagmus			
	Glioma	Glioma	.....	Partial albinism with macular loss
	Amaurotic idiocy			
	Total color blindness	.....	.....	Hemeralopia and myopia
				One form of myopia
Pupil and Lens				
	Ectopia pupillae	Aniridia	Iridic and other coloboma	Atrophy of iris, with glaucoma
	Ectopia pupillae et lentis	Ectopia lentis		
	Ectopia lentis	Spontaneous luxation of lens	Floceuli iridis	
	Microphthalmia	Luxation from arachnodactylia		
	One form of congenital juvenile zonular cataract	Microphthalmia with myopia and ectopia of pupil		
	Cataract with hydrocephalus and microphthalmia	More forms of cataract (also myotonia)		
Cornea				
	Keratoconus	Familial degeneracy	Microcornea	Megalocornea
	Cornea planus	Blue sclera	Astigmatism	
Muscle				
	Ptosis and muscle paralyses	Isolated ptosis	Strabismus convergens	One form of nystagmus
	Cryptophthalmus	Ptosis and blepharophimosis	Nystagmus	
	Anophthalmos	Ptosis and ophthalmoplegia		
Glaucoma				
	Juvenile with keratoconus	Distichia epicanthus glaucoma	.....	One form of microphthalmia with blindness

MAYER, Chicago. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

STUTTERING: ITS NATURE AND MECHANISM. MEYER SOLOMON, Illinois M. J. **65:** 329 (April) 1934.

Stuttering is an emotional and personality disorder. It is due to emotional disequilibrium in social situations requiring speech, with a consequent struggle to maintain or regain equilibrium and an accidental stumbling into stuttering, which may then become a conditioned emotional response in speech in social situations. The emotional disequilibrium during speech in social relations may be induced by many factors of a psychologic nature which are responsible for undue stress, strain and tension. Fear of recurrence of speech difficulty and transformation of

the personality are added later, if the stuttering continues. The scientific treatment of stuttering, therefore, according to Solomon, should be based on the conception of this condition as an emotional and personality disorder. It requires intensive study of personality and reorganization of personality. The condition should be studied and managed in its earliest phase. Stuttering arising in the preschool or school period requires careful study of the child's habits, of the technic of child management and of the home, neighborhood and school influences, searching especially for causes of undue pressure and tension. BARBOUR, Peoria, Ill.

SURVEYS ON TONSILLOGENOUS SEPSIS (CONTRIBUTION TO PATHOGENESIS, PATHOLOGY AND CLINICAL ASPECTS). L. HAYMANN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **35**:288 (March 12) 1934.

Haymann found that in about twelve thousand and five hundred necropsy records examined death following tonsillar sepsis was reported in about 5.3 per thousand. Forty-eight per cent of the patients were men, and 52 per cent, women. They ranged in age from 15 months to 74 years. Forty per cent of the deaths occurred in the third decade and 27 per cent in the sixth, seventh and eighth decades combined. In 43 per cent of the cases the sepsis developed from the right tonsil and in 47 per cent from the left, and in 10 per cent it had to be considered as arising from both sides. In general, in the presence of bilateral but unequal tonsillar infection, sepsis was more likely to develop from the more seriously involved sides. In about 30 per cent of the cases no recognizable harmful condition of the tonsils appeared to exist, but general sepsis resulted. In about 35 per cent peritonsillar or retropharyngeal abscesses were present. Edema of the glottis was observed relatively rarely, in severe cases only. In about 10 per cent of the cases the infectious process was established in the endocranium. In two cases cavernous sinus thrombosis occurred, in one instance combined with meningitis. In twelve cases there was more or less severe thrombosis of the jugular vein. In three of these cases other veins also were thrombosed. Three other cases showed phlegmons of the neck. Isolated partially purulent thrombotic processes in the region of the retrotonsillar veins were found in three cases. Mediastinitis was observed in three cases. Frequently (in about 63 per cent of all cases) metastases occurred. These were located most often in the lungs and less frequently in the kidneys, spleen, prostate, bladder, testicles and heart, in the order named. The soft tissues and joints were affected by metastases in only about 10 per cent of the cases. Bacteriologically, the usual purulent cocci were observed, for the most part. In 20 per cent of the cases no organisms were observed; in 68 per cent, streptococci, some growing anaerobically, were obtained. The duration of illness after the onset of septic symptoms was less than two weeks in 72 per cent of the cases.

The author suggests a method of classifying the modes of origin of tonsillogenous sepsis: (1) by direct entrance of the causative agent into the blood stream without preexisting thrombophlebitis, from isolated thromboses of the retrotonsillar veins or from progressive jugular thrombosis; (2) by indirect entrance into the blood stream by way of lymphangitic or lymphadenitic changes, and (3) by phlegmonous changes, especially in the interstices of the neck, with secondary thrombosis of the veins, especially the jugular. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OPERATIVE TREATMENT OF SO-CALLED DIAPHRAGM OF THE LARYNX. K. BECK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **35**:303 (March 12) 1934.

The case of a girl, aged 16, with shortness of breath on exertion and hoarseness due to a membranous formation in the larynx is described by Beck. After two unsuccessful attempts to relieve the condition an operation was performed. Under local anesthesia a collar incision was made (for cosmetic reasons) and the larynx opened. The membrane was pushed aside with the knife, and a rubber tube was placed in the trachea, extending to the lips of the larynx. This tube

was allowed to remain three weeks, after which it was removed and the incision closed. Eleven months later the glottis remained free, and there was good scar formation on the anterior commissure. The patient was much improved, though the voice retained a hoarse note. The author believes that this method can be recommended.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

EXCESSIVE SOLAR AND PHOTOTHERAPEUTIC IRRADIATION: A CAUSATIVE FACTOR IN CERTAIN DISEASES OF THE SKIN. PAUL E. BECHET, Arch. Dermat. & Syph. **29**:221 (Feb.) 1934.

Bechet emphasizes the many harmful effects from overexposure to the actinic rays, whether natural or artificial. Among the diseases of the skin caused by overirradiation are epitheliomas, disseminated lupus erythematosus, so-called war melanosis, cutis rhomboidales nuchae, herpes facialis and erythema multiforme. Psoriasis and syphilis may be made much worse by severe sunburn. Even death has been reported from overexposure to a "sun lamp." Bechet believes that special effort should be made to inform the layman of the dangers of too much exposure to the actinic rays.

DULIN, Iowa City.

BLOOD LIPIDS IN XANTHOMA. JEFFREY C. MICHAEL and H. O. NICHOLAS, Arch. Dermat. & Syph. **29**:228 (Feb.) 1934.

Michael and Nicholas discuss the theory of the pathogenesis of xanthoma and present a series of three cases of xanthoma multiplex and five of xanthoma palpebrarum. In their chemical studies of these cases the following data were recorded: the total lipid, with its partition consisting of cholesterol, phosphatides and neutral fats, fatty acids and soaps, and also the percentage of cholesterol ester to the total cholesterol. In all the cases they found a disturbance between the relationship of the lipid constituents or in the cholesterol ester-free cholesterol ratio. They believe that there is some factor besides this which, by making the oil-water emulsion of the blood unstable, allows xanthoma to develop. Whether this is other constituents of the blood or some substance in the tissue at the site of formation of the xanthoma is an open question; they are making further studies at present.

DULIN, Iowa City.

RADIUM NEEDLES IN TREATMENT OF ANGIOMAS. A. MARIN, Union méd. du Canada **43**:169 (Feb.) 1934.

Marin discusses forms of treatment of angiomas other than irradiation, but rejects them as ineffective, scar-producing or painful. Surface irradiation has the danger of producing a dermatitis if the tumor requires many applications. If radium needles are buried in the growth the necessary endarteritis is produced without damage to the skin. In cases of angioma of the mouth or the genital mucosa this treatment is the only feasible one, because of the inapplicability of surface irradiation. No untoward results were observed in any of Marin's cases.

DAFFINEE, Boston.

FAMILIAL SEX-LINKED ECTODERMAL DYSPLASIA WITH INCOMPLETE FORMS. R. E. CLARKE and R. A. MCCANCE, Arch. Dis. Childhood **9**:49 (Feb.) 1934.

A typical case of ectodermal dysplasia in a boy, aged 14 years, is presented. There were but five teeth. The maternal grandfather and a great uncle had deficient sets of teeth, which makes the condition one of the sex-linked recessive type. The boy's teeth did not erupt until the age of 5 years. Roentgenograms showed no trace of other teeth, of tooth germs or of empty sockets.

KELLY, Milwaukee.

PAPULAR URTICARIA AND THE DYNAMICS OF SKIN SENSATION. D. W. WINNICOTT, Brit. J. Child. Dis. **31**:5 (Jan.-March) 1934.

In this article Winnicott develops his two theses: 1. Papular urticaria is a normal cutaneous phenomenon, a cutaneous excitement corresponding to the erection of excited erectile tissue. 2. When papular urticaria is a distressing disease there is usually a complicated psychologic disorder corresponding to obsessive onanism, in which the skin generally has become the battle-ground of a fight, chiefly unconscious, between an urge demanding gratification and a sense of guilt which threatens to deprive the child (ego) of an entire pleasure system.

LANGMANN, New York.

KAPOSI'S VARICELLIFORM ERUPTION. W. H. BROWN, Brit. J. Dermat. **46**:1 (Jan.) 1934.

Brown quotes an abstract from Kaposi's book describing a rare type of eruption which occurs as a complication in infantile eczema and reports a case in an infant aged 9 months. He states that only a few cases have been recorded after Kaposi's report of ten cases and that he has found no report in the British or American literature.

The salient features in the reported cases are as follows: 1. The condition occurs in infants with eczema. 2. The onset is sudden, with elevation of temperature and pulse rate for at least twenty-four hours before the eruption appears. 3. The eruption develops with great rapidity; a large crop of lesions may appear overnight, and they are most profuse on the face and head. 4. There is high fever for one or two weeks, the temperature ranging from 102 to 104 F., with a fall by lysis. The pulse rate shows a corresponding rise to from 130 to 150. There was no marked prostration in the case recorded. 5. The clinical features of the eruption are described as varicelliform, vacciniform or varioliform. 6. Complete resolution takes place in the majority of cases, though Kaposi and Juliusberg have each recorded a death. 7. Kaposi and others have mentioned the presence of diffuse edema of the skin, in addition to the eruption, and this was present in the case reported. 9. Some degree of pitting, as noted in variola, seems to be a feature. Two excellent photographs accompany the article.

WIEN, Chicago. [ARCH. DERMAT. & SYPH.]

LESIONS PRODUCED BY THALLIUM. A. PHILADELPHY, Dermat. Wchnschr. **98**:78 (Jan. 20) 1934.

Three cases of thallium poisoning were observed. In all three loss of hair was complete, except on the medial portion of the eyebrows. The lanugo hair was also lost. In one case sharply limited patches of erythema occurred on the fingertips, around the nails and on the dorsa of all the proximal interphalangeal joints of the hands. In all three cases transverse bands were observed on the fingernails.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

ZOSTER AND CHICKENPOX. O. THOMSEN, Hospitalstid. **77**:129 (Jan. 30) 1934.

Thomsen reviews the relation between zoster and chickenpox. He employed the complement-fixation test in eighty-eight cases of zoster and fourteen cases of chickenpox, with uniformly negative results.

ELGHAMMER, Chicago.

Surgery and Orthopedics

SURGERY OF THE THYROID IN CHILDREN. WILBUR L. BOWEN, Illinois M. J. **64**: 277 (Sept.) 1933.

According to Bowen, the earlier the diagnosis is made in cases of a hypothyroid condition the better the results of treatment are. In delayed treatment of

this condition more can be expected in the improvement of the physical state than of the mental state. Exophthalmic goiter appears in children, in whom it is a more treacherous disease than in adults. Less gland should be removed at operation on children than in operation on adults. Bowen states that goiter in adolescents is not a normal physical enlargement but may be considered an indication of future thyroid trouble and should be properly treated and watched.

BARBOUR, Peoria, Ill.

PRINCIPLES TO BE OBSERVED IN THE TREATMENT OF CONGENITAL HARELIP AND CLEFT PALATE. V. B. HYSLOP, Wisconsin M. J. **32**:246 (April) 1933.

Operative failures in from 70 to 80 per cent of the cases indicate that surgical correction of congenital harelip and cleft palate is difficult. In cleft palate, instead of weaning and artificial feedings, Hyslop encourages lactation and gives the breast milk with a Breck feeder. Special nipples to block the palatal fissure are not very satisfactory. Closure of the fissure of the lip by strapping with adhesive tape aids deglutition. The infant should be operated on only when the weight curve is going up, the coagulation time is 3 minutes or less, the hemoglobin is 65+ per cent and no acute infection or untreated persistent thymus is present. The younger the infant the better the results of operative correction of harelip, the ideal age being the first two or three days after birth. The first operation for palatal closure is done from nine to twelve months after correction of the harelip, regardless of the age at which the lip was corrected. This delay causes narrowing of the fissure. Fundamental facts to be considered in the surgical technic and types of operation on the palate are mentioned, the method of G. V. I. Brown being favored.

JANNEY, Wauwatosa, Wis.

A CONTRIBUTION TO THE STUDY OF PULMONARY LOBECTOMY. A. GRAHAM BRYCE, Brit. J. Surg. **21**:560 (Apri) 1934.

In certain cases in which lobectomy is required dense pleural adhesions often interfere with the operation. It is suggested that these more formidable cases might be dealt with by ligature of the pedicle of the lobe, the gangrenous lung being left in situ until it begins to separate by a line of demarcation between the living and the dead tissues. This article describes experimental work done on cats to estimate the ability of the animal organism to tolerate the presence of a mass of dead lung in the thoracic cavity. A detailed description of the experimental work is given, and it is shown that animals can survive in spite of a mass of dead lung in the pleural cavity.

SUMMERFELDT, Toronto, Canada.

SCOLIOSIS OF COSTAL ORIGIN. M. NAGEOTTE-WILBOUCHEWITCH, Bull. Soc. de pédiat. de Paris **31**:18 (Jan.) 1933.

A number of cases of scoliosis are discussed to support the belief that this deformity may be present without any primary deformity of the spine. In such cases malformation of the ribs, usually congenital, produces the scoliosis. Lantern slides are shown to illustrate some of the cases. In the discussion it is pointed out that rickets in early life may be responsible for spinal deformities as the child grows older, a point which the author fails to consider in the paper.

BENJAMIN, Montreal, Canada.

A CASE OF PNEUMOCOCCIC EMPYEMA; TREATMENT WITH OPTOCHIN AND SURGICAL INTERVENTION. M. BESSON, Bull. Soc. de pédiat. de Paris **31**:32 (Jan.) 1933.

A girl, 12 years of age, had empyema following pneumonia. She was given three injections of optochin into the pleural cavity, but pneumococci persisted in the pleural exudate, and her condition became worse, necessitating thoracotomy. Following this she recovered.

BENJAMIN, Montreal, Canada.

BARIUM ENEMA IN INTUSSUSCEPTION; FIVE NEW CASES; THE CLINICAL SYNDROME OF ILEO-ILEAL INTUSSUSCEPTION. MARCEL FÈVRE, Bull. Soc. de pédiat. de Paris **31**:144 (March 21) 1933.

Supplementing a previous communication on a series of infants with intussusception who were examined roentgenologically after the instillation of barium sulphate solution in the rectum, Fèvre reports five new cases, making a total of twelve in which the patients were examined in this manner. The fluid is introduced slowly at a pressure of from 60 to 80 cm. A characteristic filling defect of the intestine, at the head of which is a cup-shaped niche, can usually be identified, and the site of the invagination can thus be located. In one case the intussusception was found to be reduced spontaneously after the administration of a barium sulphate enema. Ileo-ileal invagination can be differentiated clinically from the ileocolic and ileocecal types because it readily becomes strangulated and remains short; the abdominal pains are less marked; blood appears in the stool in smaller quantity and much later in the illness, and on rectal examination the finger does not reach the mass. It is usually the most difficult type to diagnose.

BENJAMIN, Montreal, Canada.

CONGENITAL HYPERTROPHY OF THE NECK OF THE BLADDER; OPERATION AND CURE IN A CHILD OF SEVEN YEARS. M. BOPPE and J. E. MARCEL, Bull. Soc. de pédiat. de Paris **31**:315 (July 11) 1933.

A boy, 7 years old, had hematuria and paradoxic incontinence, but no pain. He had always wet his bed and clothes, and as far back as the mother could recall he had never been dry. He had been treated for enuresis. The bladder was enormously dilated, and on further urologic examination it was found that both ureters were dilated at their lower parts, the left ureter much more than the right. A retention catheter was inserted, and suprapubic cystotomy was done, as well as resection of the neck of the bladder, as this was hypertrophied. It took some months before the suprapubic incision was entirely closed and the child voided normally. The dilatation of the bladder disappeared, and the urine, which had been markedly purulent, cleared up entirely. Histologically, the neck of the bladder showed marked hypertrophy of the muscularis, which is believed to be a congenital abnormality similar to congenital hypertrophic pyloric stenosis. It is emphasized that every child with urinary incontinence and pyuria should not be considered as having simple enuresis, but should be subjected to a careful and thorough cystoscopic and urographic examination to determine whether any abnormality of the urinary tract is present.

BENJAMIN, Montreal, Canada.

CONGENITAL DISLOCATION OF THE KNEE. D. P. R. KEIZER, Nourrisson **21**:359 (Nov.) 1933.

A case of bilateral anterior dislocation of the knees was observed in a native Javanese infant aged 3 months. This was not associated with other bony anomalies. There were no signs of congenital syphilis. The early and later treatment is discussed.

MCCLELLAND, Cleveland.

STRANGULATED HERNIA IN A PREMATURE INFANT. P. HENRIET, Nourrisson **22**: 99 (March) 1934.

A strangulated inguinal hernia occurring in a premature infant weighing 1,910 Gm. was successfully reduced by taxis. In order to facilitate the reduction the infant was suspended with the head dependent. Injections of dextrose and blood transfusions speeded the recovery. The baby was breast fed.

MCCLELLAND, Cleveland.

A Case of Renal Calculus. R. Gantes and A. Guzman, Arch. de hosp. d. niños, Roberto del Rio **4**:70 (June) 1933.

Gantes and Guzman report a case of multiple calculus of calcium oxalate of the renal pelvis, associated with pyonephrosis and hydronephrosis.

Sanford, Chicago.

Roentgenologic Investigation of the Appendix in Children. Martha Rosenberg, Kinderärztl. Praxis **4**:16 (May) 1933.

In twenty-two children without gastro-intestinal symptoms the appendix was clearly outlined by a contrast medium. In sixty-five children with gastro-intestinal symptoms roentgen diagnosis of appendicitis could be made in many cases. The appendix was pronounced normal if it was normally situated, freely movable and had a smooth contour, and if it clearly filled with the contrast medium and emptied about the same time as the large intestine. Chronic appendicitis was diagnosed if the appendix was immovable, kinked and hazily outlined, and if it was the only part of the gastro-intestinal tract to retain the contrast medium for a long period (more than ninety-six hours). It goes without saying that this roentgenologic diagnosis must be confirmed by clinical evidence.

Huenekens, Minneapolis.

Bacillus Cloacae Empyema. H. Gerhartz, Med. Klin. **29**:1546 (Nov. 10) 1933.

An epileptic patient smeared himself with feces and subsequently had a pulmonary and pleural infection which resulted in empyema formation. Recovery followed rib resection. The pus contained Bacillus cloacae.

Dooley, New York.

Miscellaneous

American Academy of Pediatrics in the State of Illinois. George Edwin Baxter, Illinois M. J. **64**:525 (Dec.) 1933.

As chairman of the Illinois committee, Baxter reviews the activities and plans of the committee for carrying out the aims and objects of the American Academy of Pediatrics as they apply to Illinois. The activities consist of the application for a section on pediatrics at the annual meetings of the state society and the prompt granting of this by the House of Delegates; the immediate organization of a pediatrics section and the appointment of officers to arrange for the program of the first meeting; the appointment of a subcommittee the duty of which shall be to contact all the governmental agencies throughout the state for the purpose of aiding or advising these agencies in matters pertaining to the welfare of children; the appointment of a committee to contact various lay organizations throughout Chicago and the state for the purpose of advising the members of these organizations and attempting to direct their activities from a medical standpoint, and the drawing up of pediatric programs or postgraduate courses to be offered and presented to groups of county societies and branch societies of the Chicago Medical Society.

Barbour, Peoria, Ill.

The Skin Reaction to U-V Radiation. P. R. Peacock, Brit. J. Phys. Med. **8**:173 (March) 1934.

The author concludes that if it is desired to obtain the maximum absorption of ultraviolet rays by the skin of a patient it is necessary to avoid marked reactions with consequent pigmentation and thickening of the horny layers. He bases his conclusions in part on studies of the fluorescence of the different layers of epidermis in sections of the skin.

Hartman, Cleveland.

THE INTERACTION OF HEREDITY AND ENVIRONMENT. LANCELOT HOGBEN, J. Ment. Sc. **79**:590, 1933.

The contributions of genetics to the study of social phenomena, including mental disease, are discussed in this article with intelligence, understanding and thoroughness. Advances in science are determined not only by the ability to ask questions but by the development of technics for answering them. The fact that the condition is congenital does not mean that the environment is of no etiologic significance. The intra-uterine environment has not usually been taken into consideration. The importance of intra-uterine environment is indicated by the high incidence of malformation in children born of mothers approaching the menopause and the frequency of certain conditions in first-born children. When the modus operandi of the genes is understood one will know the kind of knowledge needed to control the influence of the genes. Selection is not the only way in which heredity can be controlled. Hemophilia is a hereditary disease, but with ovarian hormone therapy it can be controlled in spite of the innate tendency for it to occur. The knowledge of the way in which one dominant gene produces its manifestations teaches how to prevent or further these manifestations. The same gene may be responsible for several varied traits. A great deal depends on the way in which the genes are combined. Thus, when two kinds of tropical fish are combined for the purpose of producing a new, more decorative breed, the effect is easily achieved, but there also develops a certain tumor which was apparently carried as a recessive in the same gene which controlled pigmentation. When the method of genetics is transferred intelligently to psychiatry, interesting results are observed. Thus, Penrose (*J. Genetics* **25**:407 [April] 1932) found that the frequency with which mongolian idiots are born of mothers over 40 years of age compares to the theoretical 1 : 3 ratio, if one takes into consideration that mongolian idiots are likely to die before birth. Mental defect is not a unitary character. It is essentially a tail-end of a normal distribution of intelligence. It is a sociologic rather than a clinical concept. The freudian school performed a service to human biology by focusing attention on the importance of the social environment. In mental disease different mutations and different environments in different situations may be chiefly responsible for the same clinical entities. Mental disease, thus, is not a genetic problem alone; neither is it a single genetic problem. The division of disease into two groups, mental diseases which are due to heredity and bodily diseases which are due to environment, is a legacy of that period in the history of science when the study of the central nervous system belonged to the province of moral philosophy.

KASANIN, Howard, R. I. [ARCH. NEUROL. & PSYCHIAT.]

ULTRA-VIOLET IRRADIATION IN TREATMENT OF DISEASE. ROBERT STANTON WOODS, Practitioner **132**:132 (Feb.) 1934.

The author comments on the recent "exacerbation of irradiation" and deplores the fact that its proper value has never been assessed.

The physical basis underlying ultraviolet irradiation is described in detail, beginning with the modern view of what constitutes matter. A rough guide by Eidinow as to the depth of penetrability of rays of different parts of the spectrum is given. The "near" ultraviolet group of rays occurring in the middle of the "erythema-producing" band (from 3,300 to 2,500 angstrom units) with which this article deals are of little penetrating capacity, reaching only the living epidermis. This group constitutes the radiation possessing antirachitic properties.

The two main theories as to the action of these rays, when absorbed, are reviewed; the obvious effect on the skin is described, and the chemical changes of therapeutic value (including elaboration of vitamin D) are discussed.

Direct and possible indirect bactericidal actions, the relationship between calcium-phosphorus metabolism and the action of "near" ultraviolet rays and the indications and contraindications for therapy are reviewed.

The author considers the principles of technic laid down by Eidinow as rational as any. These principles are given briefly, followed by a description of the author's "less scientific," but "not unsatisfactory" technic, consisting of general exposures, beginning with a minimal dose.

SAPPINGTON, San Francisco.

EXTRA-UTERINE PREGNANCY; OPERATION IN THE NINTH MONTH, WITH SURVIVAL OF MOTHER AND CHILD. E VAYSSIÈRE, Bull. Soc. d'obst. et de gynéc. **23**:240 (March) 1934.

Extra-uterine pregnancy extending into the sixth month is uncommon, and that ending near term, with survival of both the mother and child, is extremely rare. The case reported is that of a woman, 35 years of age, who had previously had six pregnancies, only three of which resulted in living children. The course of this pregnancy was stormy, but the diagnosis of ectopic gestation was not made until the ninth month. At this time an operation was decided on, in the hope of obtaining a viable infant. The child was found practically free in the abdominal cavity. The placenta was situated in the left iliac fossa. There were several intestinal adhesions, which were liberated without great difficulty. The infant weighed 2,200 Gm. and developed normally on bottle feedings.

GLASER, Rochester, N. Y.

TREATMENT OF ACUTE LUMINAL POISONING. G. CARRIÈRE, C. HURIEZ and P. WILLOQUET, Gaz. d. hôp. **107**:745 (May 23) 1934.

Sublethal and lethal doses (from 0.08 to 0.21 Gm.) of phenobarbital were injected into dogs and rabbits. Of the five untreated animals only one survived; this had received only 0.08 Gm. Of the seven animals treated with strychnine four survived; all six of the animals given an intravenous injection of 30 per cent alcohol were saved, but the coma lasted for seventeen hours. Five animals were treated with coramin; all were saved, and the coma lasted for only five hours.

The treatment that the authors advocate consists of lavage with dilute permanganate of potassium, injections of caffeine or hypertonic dextrose to combat the low blood pressure and the intravenous injection of 30 per cent alcohol or coramin as a physiologic antidote.

KAJDI, Baltimore.

THE SUSPENSION OF YOUNG INFANTS. JOSÉ OBES POLLERI, Consejo de Salud Publica, Montevideo 1933.

For the past eight months approximately 100 infants have been hung in a suspension apparatus at the Casa del Niño. The babies are strapped in an upright position and are suspended from a wire by a hook. This vertical position is presumed to aid digestion and is an effective means of combating infections of the respiratory tract. In twenty-seven infants who were suspended the mortality from bronchopneumonia was 7.4 per cent, while in twenty who were not suspended it was 50 per cent.

SANFORD, Chicago.

PREMATRIMONIAL CONSULTATIONS. ERNÖ DEUTSCH, Paidoterapia **12**:763 (Dec.) 1933.

The author presents the evolution of modern infant protection, the protection of the preschool and school child, with the development of the modern pediatric feeding procedures, on a charitable basis, and finally the prematrimonial consulting institution, on a eugenic basis. He believes in social hygiene for all classes and discusses the quantitative and qualitative eugenic principles concerning the birth rate, from the economic and the moral point of view. He states that birth control is necessary and that sterilization of the unfit is demanded. Every one should be eligible to receive information regarding contraception.

HERRON, Spokane, Wash.

EARLY SYMPTOMS OF CONSTITUTIONAL INFERIORITY IN CHILDHOOD AND ITS SIGNIFICANCE IN THE IMPROVEMENT OF THE RACE. BECK, Arch. f. Kinderh. **101**:129 (Feb. 28) 1934.

For the improvement of a nation persons who are physically and mentally sound must be encouraged to reproduce, while inferior persons must be prevented from bringing into the world children who are not equipped to become an asset to the community. The practicing physician is in a position to recognize signs of constitutional inferiority in infancy and early childhood and to advise against the parents bearing any more children. The author discusses the common symptoms and stigmas of hereditary deficiency such as are found in neuropathic infants and psychopathic children, feeblemindedness, mongolian idiocy, alcoholism and epilepsy. By early recognizing signs of constitutional inferiority in children and by restraining the parents from further reproduction, definite improvement in the stock of the race can be confidently predicted. LEMASTER, Evanston, Ill.

IMMUNITY OF THE INFANT. IVO NASSO, Kinderärztl. Praxis **4**:1 (Jan.) 1933.

Other things being equal, the breast fed infant has greater resistance to infection than the artificially fed infant, though the ultimate cause of this is not clear. Interesting is the immunity of infants to the exanthems, especially measles, German measles and scarlet fever. It has been widely assumed that this immunity is passive and that it is due to the placental transfer of antibodies from the mother. This does not explain the cases in which the mother herself contracts measles (thereby showing that she had no antibodies to transfer) and the infant apparently does not contract the disease. Nasso's explanation is that this is due to the lack of reactivity of the infant's skin; many infants contract the exanthems, but without the characteristic cutaneous manifestations. The negative Schick reaction in infancy, even though the infant may be susceptible to diphtheria, and the mild local reactions to successful vaccination may be further manifestations of the lack of cutaneous reactivity. This lack of reactivity is probably largely due to the anatomic and physiologic immaturity of the skin's circulatory apparatus, as shown by the capillaroscope. The behavior of the bullous conditions of the newborn (pemphigus, dermatitis exfoliativa and erythrodermia desquamativa) is partly explainable on the basis of the immaturity of the capillary system of the skin; The cutaneous reactions do not give a true picture of the immunity of the infant; an exception must be made of the skin test for tuberculosis, which rests on an entirely different basis. HUENEKENS, Minneapolis.

NEW METHODS OF TREATMENT IN AMERICA. E. GORTER, Maandschr. v. kindergeneesk. **3**:18 (Oct.) 1933.

The author discusses some newer methods of treatment as yet not applied in Holland, which he saw and discussed during his journey in America. These include the treatment of chorea minor by artificial fever, the treatment of myasthenia gravis and muscular dystrophia with large amounts of glycine, the treatment of stenosis of the larynx in diphtheria by sucking away the membrane, the use of the Drinker respirator in serious cases of Heine-Medin's disease, the treatment of gonorrheal vulvovaginitis by theelin, the treatment of diseases of the lungs with dyspnea and of cyanosis by the inhalation of oxygen, the air-conditioned room of Blackfan in Boston for premature children, the treatment of toxicosis by the continuous intravenous injection of fluids (Schick-Karelitz) and the ketogenic diet in urinary infections. VAN CREVELD, Amsterdam, The Netherlands.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Dec. 13, 1934

HARRY BAKWIN, M.D., *Chairman*

ALEXANDER T. MARTIN, M.D., *Secretary*

INTELLIGENCE TESTS IN RELATIONSHIP TO YOUNG CHILDREN. DR. JOHN LEVY.

From the pediatric point of view intelligence tests of young children are especially unsatisfactory. Up to now psychologists have evolved no short-cut methods which are scientifically accurate for testing the intelligence of very small children. An adequate test of the 3 year old child takes from thirty to sixty minutes. The results of such tests remain tentative. One should be more impressed by the positive findings than by the negative findings; that is to say, a child who is found to be especially bright in the tests is likely to be bright as he grows up, while the child who does poorly in these tests is not necessarily dull. The external conditions under which a child takes the tests, the psychologist's personality or the child's normal negativism may vitiate the results. As the child reaches the ages of 5, 6 and 7, the results are more reliable; moreover, for children of these ages testing procedures can be abbreviated.

In spite of this somewhat discouraging point of view with respect to testing the intelligence of young children, there are certain short-cut objective measures which can be used for making a better rough guess of the child's intelligence than the usual hit or miss methods used by pediatricians. I refer to the Gesell development scale, the Kuhlmann series of tests, the Goodenough drawing test and the Merrill-Palmer School series of intelligence tests for young children. From this battery one can select more significant tests and obtain a fairly reliable but tentative estimate in a reasonably short period.

PSYCHOLOGIC CARE DURING EARLY CHILDHOOD FROM THE STANDPOINT OF THE PEDIATRICIAN: HABIT TRAINING. DR. LAWSON G. LOWREY.

A 34 year old mother brings her 4 year old son to a pediatrician because he has become "unmanageable." She complains that he is overactive, has temper tantrums, does not play well with other children, is a cry-baby, will not fight, cannot be made to go to bed early at night, is finicky about his food and, especially, that he attacks all the adults with whom he comes in contact. These, according to her, are habits. In other words, this is the way he responds to all situations in which response of a certain type is to be expected. She does not complain of some of the common problems that are brought by parents to the pediatrician. For example, there is no enuresis; there has so far been no masturbation, and there is no thumb-sucking. However, two of the five problems most commonly presented to the pediatrician, namely, food fads and temper tantrums, are present. Added to that there are other habitual modes of response that are creating trouble for her. Where will one look for the origin of these habit problems which disturb her?

I recently looked up the definition of habit. It is defined very inadequately in most dictionaries. A habit is simply something that is done more or less constantly

in response to a given stimulus. The development of habits depends on the stage of development of the individual in terms of the physiologic and neurologic possibilities for the development and maintenance of habit patterns.

In the case of a child who has clean toilet habits at the age of 6 months, what would be the line of approach to the analysis of that problem? In the first place, without seeing the child one is fairly certain that there has been accelerated physical development, plus a consistent day by day and hour by hour training pattern established within the home to permit this accelerated habit development. But this child's brother, at the age of 4 years, still has enuresis, both diurnal and nocturnal. By careful tests and physical examination he is found to be both physically and mentally accelerated. The mother explains that with the first child she had nothing else to do but pay attention to the development of proper habits, but with the second child she did not have time.

Another child at the age of 22 months has fully developed language habits and fully developed motor habits, is not awkward and has a visual memory enabling him, once he has seen an alphabet block, to tell what is on the other faces when one face of the block is shown. One would expect an equal acceleration of the development of habits, but the home situation causes a great deal of interference because of emotional factors.

The general principles of the investigation of habit problems as they are presented to the pediatrician can be laid down rather simply in this way.

There are norms as to what habit formation should be at different ages in infancy and early childhood. Until recently they have been inadequate, but more precise, statistically reliable observations on the rates of development and the time of development of different sorts of habit patterns are becoming available. If one is seriously interested in the problem, I should recommend reading "Infant Behavior" by Gesell and Thompson and Gesell's previous books on the growth and development of the infant, also, Baldwin's book on the same topic. There one will find a valuable mine of information derived from direct and controlled observation, which may do a great deal to clear up some of the confusion based on clinical observation of children under widely varying circumstances, where one is not able to have sufficient controls to be certain of the value of one's observations.

If one finds no physical disorder to explain the anomaly of habit, one must consider the physiologic rate of development—retarded, average or accelerated. There may be various discrepancies in physiologic development which may have an important bearing on the particular habit problems.

The third line of investigation relates to the home setting, particularly the relationship between mother and child. The mother's idea as to the rate of child development, her expectations at a given time and her emotional attitude toward being a mother present problems.

The case which I cited in introducing my comment works out in this way: The child, who is of superior intelligence and physiologically somewhat accelerated in development, presents no problems of physical disorder, but presents problems of social adjustment related distinctly to the fact that his mother feels that she should never have married, feels no maternal urge but consented to have a child because her husband wanted it and speaks of this child's behavior as though it were comparable to that of an adult. She said that he was impatient to get his own way and was obstreperous if he did not. She said that she was impatient too, but had learned to control herself. In other words, what she said was: "Why isn't he as old as I am?" This is a rejecting mother. She brings pressure to bear on the child to be more adult. The child exhibits a healthy rebellion against this pressure.

So-called food fads have a rational origin in many cases. Idiosyncrasies and dislike for the taste of a particular food are a sound basis for such fads. The experiments carried out in Cleveland showed that small infants allowed to make their own selections of food got nicely balanced diets and were just as healthy as

those who had their diets selected for them. Respect for children's tastes, within the limits of health, of course, makes for less difficulty in regard to food. However, certain adults in the family may have definite dislikes and fads in regard to food, and the child may imitate their food habits. This problem must be gone into in deciding what the child should eat.

Feeding problems arise in early infancy. Parents worry about physical development and weight. They early try forced feeding. This starts a psychologic battle between parents and child which extends into other fields, because it usually occurs before the development of the peak of negativism. When the negativistic period comes and the child begins to assert himself in opposition to the parents' pressure and wishes, not only this but other problems will be accentuated.

The principles of investigation of food fads apply also to temper tantrums. Are they by any chance epileptic manifestations? I teach my students to think of epilepsy first, because they may forget it otherwise. The chances are that the condition is not epilepsy. If it is not, is there a basis for physical irritation, such as chronic fatigue, or is there a mild chronic disease? Do the physical findings account for the heightened irritability? What, for example, is the constitutional status as related to the thymus? What is the state of the metabolism of various minerals? What is the general metabolic rate?

My experience has been that, in general, there is a combination of various constitutional and mild physical factors with factors of irritation arising in one way or another from the environment.

Commonly the irritation due to the environment arises because the parents, teachers, physicians and others have not made a wise adaptation of whatever it is they are trying to carry out to the personality make-up and peculiarities of the child with whom they are dealing. I maintain that the child, as well as the adult, has a right to a few personal peculiarities, and that these should be respected by those with whom they are in contact.

The problems of habit formation are not quite as simple and discrete as I have intimated, but I cannot go into the whole process of habit formation in the short time allowed me tonight. All that I plead for is this: Try to look at these habit problems from the physical, developmental, mental and social standpoints. Finally, ask yourself this question, no matter how bad the problem may seem to be: "What satisfaction is this child deriving from this deviation of habit pattern from that which should be normal and acceptable to his parents?" Something satisfying to the child will always be found!

EMOTIONAL BEHAVIOR DURING EARLY CHILDHOOD FROM THE STANDPOINT OF THE PEDIATRICIAN. DR. IRA S. WILE.

Pediatrics is that branch of medicine concerned with the hygienic care and the treatment of diseases of children. Unfortunately, the traditions of medicine have placed primary concern on the physical problems peculiar to childhood rather than on the child. The pediatrician should be interested in the whole child. He should recognize distinctive characteristics in children, whether these are inherited or acquired. He should differentiate the hypokinetic from the hyperkinetic child and be familiar with the neurotic child who manifests fears or phobias and reacts with somnambulism and anxiety states. He must appreciate that in early childhood there are many forms of behavior which may be termed emotional, varying from manifestations of frustration to neurotic maladaptations.

The early differentiation of juvenile types is advantageous. The difference between the seclusive, sensitive introvertive child and the happy extravertive child is important. All forms of emotional behavior, including those of infancy, serve to defend the ego goals of the child. They are indicators of an adaptation technic of far more than the level of intelligence.

Emotional behavior is of significance to the pediatrician, because it is a unifying factor in childhood reactions and is not independent of intelligence but enters into intellectual activities and all habit forms. Whatever affects the intelligence quotient, whether it is functional or organic, modifies the entire child.

Normality at any age must involve the balance of all the component forces entering into the psychic life. Tonsillar diphtheria as a local cause disseminates its toxic effects, but a single fright and its concomitant emotional reactions may destroy continence of urine and feces. Irritability is as much a part of the child as a whole as it is characteristic of protoplasm.

It is obvious that emotions exist in early life, although with less elaboration and direction than during later childhood and adolescence. Early infantile behavior is characterized by maximal uncontrolled emotional trends. All emotional behavior is symptomatic. Pain as emotion inhibits; pleasure stimulates; but in extremes these forms of behavior may be reversed. The overt expression depends on the degree of organization of the experience of the child and the level of responsiveness to new situations.

An appreciation of infantile behavior involves an understanding of the nature of the child organization and his relation to his parents, teachers and physicians.

Pediatricians face the emotional life of children in every effort at physical examination. Emotional behavior can never be ignored, as emotional reactivity is one index of vitality. The pediatrician is accepted as an authoritative guide concerning the growth of children and their functional development. Emotional behavior may eventuate as psychogenetic chorea, single or multiple tics, epileptiform seizures, asthmatic attacks, tantrums, enuresis and other manifestations.

The various theories of emotions need not disturb the pediatrician, although familiarity with them may be helpful. An appreciation of the meaning of multiple causation and multiple effects from single simple causes is, however, of paramount clinical importance.

The pediatrician has ample reason to broaden his concept of the child as a unitary reacting organism in terms of emotional organization and tensions.

Emotions, despite their relations to visceral and endocrine activities, are not localized. They represent functional phases of integrated activity. All behavior is physicopsychic, psychobiologic and psychosocial. The emotions, as dynamic driving factors, are also biologic, possessing survival value. The continuous evolution of emotional life involves several levels of reactions: the inherent automatic responsive mechanisms of infancy, the developing patterns of conscious control during childhood and the social adaptation of emotions as part of the reorganization of adolescence. Emotional behavior is part of the child's struggle for his own satisfaction in adjustment to his world.

Obviously, then, the emotional life is part of the personality under care, and this suggests the importance of early guidance toward reasonable types of emotional control.

It must be borne in mind that emotional instability may be manifested early in life and serve as the foundation of later maladjustment. The pediatrician should be familiar with the natural emotions and their range of expression in health as well as during illness. Thus only can he ascertain what emotional meaning lies behind agitation or depression. He must accept emotional activity as participating constantly in juvenile life and behavior. He must become an interpreter of child nature as well as a counsellor concerning psychologic hygienic development from birth to maturity. Recognizing that juvenile life is motivated by emotional values, the pediatrician must broaden his outlook on his opportunities and obligations to his patients. All forms of emotional behavior are the functional outgrowth of internal-external interactions established on the hereditary and environmental foundations that constitute the basis of all life. The need for essential psychologic

care should be recognized by the pediatrician who is concerned with the total care of children as integrated and whole organisms.

DISCUSSION

DR. F. ELMER JOHNSON: Since Brennemann made his timely address in Boston in 1931 on the "Menace of Psychiatry" I have noticed an improvement in the attitude of both psychiatrists and pediatricians toward behavior problems. It is encouraging that pediatricians are giving much more attention to the behavior problems of their patients. At our weekly conferences at St. Luke's Hospital, behavior problems are presented more often than formerly, and there is usually a delightful discussion, more so than with other cases. Also, more pediatricians are taking up these problems as their major interest.

I have also observed a saner attitude among psychiatrists dealing with children. They are beginning to realize that there is no behavior pattern that can be called normal. When Cameron wrote his book "The Nervous Child," he was told by his friends that the title should be "The Normal Child." He writes in the preface: "Perhaps so, but I could hardly call it 'The Nervousness of the Normal Child.'" This change represents real progress.

I have been in practice long enough to know that most of the bad habits of infancy and childhood disappear and leave no bad effects. This is true with habit tics, thumb-sucking, nail-biting and many other habits. Many of one's anxieties were unwarranted. The chastening effects of the give and take of school and social contacts eliminate many of these bad habits.

On the other hand, any deviation that affects the child's character or his social adjustment deserves a great deal of thought and time. Maladjustments at school, asocial behavior, lying, stealing and other behavior of this nature must be attended to, and usually the psychiatrist is better equipped for this work than the pediatrician. I am of the opinion, however, that it is the pediatrician's province to determine when the psychiatrist should be called in.

Many of the behavior problems are due to organic or functional disturbances. Twitching of the eyes may start from simple conjunctivitis. Enuresis sometimes has an organic basis. Night terrors may be due to too much supper or the wrong kinds of food. Many ill-mannered or peevish children are merely fatigued. These problems can and should be corrected by pediatricians.

The discouraging side of this problem is the pediatrician's inability to change the child's environment.

I have found that a large number of children with behavior problems come from homes in which the parents are separated or divorced or in which there is friction. This is particularly true when the religious and ethical standards are low. Masters of preparatory schools have told me that these children are the most difficult to handle. On the other hand, if the love life of the parents is ideal the future of the children is almost certain to be all right, even though there may be serious problems.

The summer camps have done more than any other agency to help solve these problems. I also have three schools within 100 miles (161 kilometers) of New York, where I can send young children whom I wish to separate from their parents for a week or more. They are conducted like summer camps, and the expense is nominal. Unfortunately, the children who need the change most are denied the experience by their oversolicitous parents.

I hope that some day the speakers can present the life histories of children under their care who have attained adult life. I should like to know what kind of environment and management in childhood makes for character and poise, and what makes for good citizenship, sportsmanship and culture. It will be a memorable day when these reports are published.

At every visit of the parents to the pediatrician there is an opportunity to teach mental hygiene. For example, I am sure that if one fed the young baby intelli-

gently there would be no more anorexia. This leads me to mention a condition which is very disturbing. Because of the prevalent habit among pediatricians of feeding solid foods early and of using quantitative diets in metabolic disturbances and in malnutrition, much harm is done.

I wish to illustrate this fact with 2 cases, reported briefly. These represent the more severe features of a common condition:

A girl, aged 8 months, was brought to the office on Jan. 27, 1932. She had been offered a normal diet for her age, including cereals, vegetables, broth, beef juice and plain milk four times a day. The weight was 16¾ pounds (7,597.66 Gm.), and the height 26½ inches (62.23 cm.). There were four teeth, and the tonsils were large. The baby was very irritable, and all food was forced by the nurse under the direction and insistence of the physician. The nose was held, the mouth forcibly opened and the food spooned. This had been going on for a month. For some time the baby gagged at the sight of food, and, as the nurse naïvely said, forced herself to vomit. When I prepared to wash out the stomach, I found that I could not pass the tube beyond 6½ inches (16.5 cm.) from the lips. Roentgenograms were taken after the injection of barium sulphate, one of which showed constriction at the cardia, with dilatation above the constriction. A laryngologist passed an endoscope and found an obstruction at the cardia which he believed was a congenital malformation. On several occasions he passed graduated bougies, dilating the esophagus to the normal size.

Believing the obstruction to be organic, I taught the nurse to pass a small catheter three times a day and to give a concentrated milk mixture. Finding that at times the tube would enter the stomach without resistance and at other times would stop at 6½ inches, I came to the conclusion that the condition was cardiospasm due to forcing. At this juncture we tried to separate the baby from the parents and nurse in the hospital, but the mother's love was too great to allow her to stay away, and she continued to officiate at feedings.

The family then went to Philadelphia to consult Dr. Chevalier Jackson. He wisely would not consider treatment unless the family returned to New York and left the baby in his hospital. In two days, without instrumentation, but after fasting, the child ate normally. This case is one of forcing food, with resultant cardiospasm.

A 9 month old baby was brought to the office on Dec. 5, 1931, because of vomiting for three months. He had ear trouble and refused to eat, but the doctor insisted on forcing. An elaborate diet was prescribed and the quantities of food for each day were specified. The mother followed directions, resorting to forcing, and the child gained until he weighed 21 pounds (9,525.43 Gm.) at 7½ months. The vomiting increased, and the appetite decreased. The child vomited when he saw the mother approaching with his food. Diarrhea began, and when I saw the baby, he had lost 4 pounds (1,814.37 Gm.). He refused all food, including that in bottles. He was severely dehydrated and was sent to the hospital. After a long period of diarrhea, with careful feeding and transfusions, he was discharged with a normal appetite and gaining. Allergy to milk also developed.

Dr. Herbert B. Wilcox: The pediatrician should apply to behavior problems the same reasoning that he has been trained to use in the diagnosis of organic lesions; that is, he should attempt to identify and eliminate the causative factors.

There are many theories as to the origin of functional nervous diseases in children. The maturation theory, the biologic, the endocrine or epigenetic theories do not often apply, nor do philogenetic memories or inherited reflexes explain, excuse or define the behavioristic problems commonly seen in the first decade. The theory based on conditioned reflexes serves better than most.

The thoughtful pediatrician must, nevertheless, strive to become psychiatrically minded by arming himself with a thorough working understanding of the principles of these various theories or explanations. He will, however, more often find the keynote in the pediatric literature when, for instance, he reads, "Among

the hazards commonly affecting health in childhood today are food, fatigue and fussy parents." He learns of the importance of functional nervous diseases in childhood again from the pediatric literature when he finds that at one clinic more problems due to the unfortunate reaction of adult personality on children are found than those of the purely medical nature or that next to disorders associated with tonsils and adenoids come those due to faulty management of behavior difficulties.

Confirmation of this evidence as to the incidence and etiology of childhood neuroses is found in the statement of a psychiatrist interested in childhood that the common factor in every one of 500 cases in young persons who needed psychotherapy was an unfortunate child-parent relationship. The material for this analysis was gathered in four different clinics and represented the observations of forty psychiatrists.

In the end the question is asked whether or not any child-parent relationship, from a psychiatrist's standpoint, can be called healthy. Of course the answer is in the negative, and yet the incidence of unhealthy relationships of this sort is greater than that of any other factor in childhood neuroses.

A recent analysis of the cases of 550 patients admitted to a children's clinic and of those of 1,100 patients in private practice showed that 1 per cent in the former and 10 per cent in the latter group are brought for treatment of behavior problems. In the group of those brought to the hospital many cases were, of course, overlooked. In both groups many children suffering from various disorders presented behavior problems also. The analysis, however, was made of the cases of those suffering from the latter exclusively. Sex, age, the state of nutrition, the number of siblings and heredity played no important part in either group. Faulty parental control was the important etiologic factor in three quarters of the cases seen in private practice and in one half of those seen in the hospital.

Such faulty management may consist in overcontrol or nagging or in lack of control and neglect. The results are much the same in either extreme. In all the patients there appeared a decided tendency to recover, even when the faulty environment could not be improved. The evidence is the same, whether the point of view is that of the pediatrician or of the psychiatrist. The method of attack must also be the same.

The responsibility may be said to lie with the pediatrician so far as it has to do with food and fatigue, and with the psychiatrist as regards the education and training of potential parents. It should come back again to the pediatrician when parenthood is an accomplished fact and has made application to the child possible.

Illustrative cartoons were demonstrated.

Dr. John Levy: A verbal barrage seems to have been laid down for the psychiatrist tonight. I am glad to hear it, even though I escaped the attack only because my phraseology was understandable. The pediatrician has a great deal of latent antagonism toward the psychiatrist. I am anxious to see this feeling come out in the open; hence my pleasure with the barrage. Having had training in both pediatrics and psychiatry, I feel justified in coming to the defense of psychiatry. Not that it needs any defense. It has a history of respect for scientific method and a disciplined experimental point of view which should command respect in return.

The impression has been given here tonight on the part of the pediatricians discussing the papers that the psychiatrist knows about and is interested in only abnormal children. This is incorrect. Child guidance work has become so generally accepted by the layman that the expert in child guidance, both in the clinic and in the private office, has had during the last few years a wide opportunity of seeing the same kind of material that the pediatrician sees. In my own clinic at the Medical Center, for example, most of the time is spent in working out such problems as enuresis, temper tantrums, food difficulties, sleeplessness, overactivity and thumb-sucking. These are essentially the same problems that come to the

attention of the pediatrician. Not more than 1 per cent of our public or private practice is concerned with the truly abnormal child.

There is another point on which I should like to take serious issue with the pediatrician: The pediatrician has a laissez-faire attitude toward children's behavior problems. More frequently than not he tells the mother to leave the child alone, that he will grow out of his difficulties. (This attitude on the part of the pediatrician is sometimes due to the fact that he does not know what to do about the problem.) This advice might be good if the mother could follow it and the child actually did grow out of its difficulties. Unfortunately, the mother is not able to follow this suggestion. As a rule, she is so tied up with the child's symptoms that she has a drive to stir up the very behavior for which she appears to be seeking help. But, more than that, while it may be true that the child grows out of his symptoms he does not necessarily grow out of his problem. The thumb-sucking, enuresis and feeding difficulties which the child leaves behind as he grows older may turn into severe personality difficulties later on. The thumb-sucking and temper tantrums may represent underlying personality maladjustment, which the pediatrician, who was interested only in treating the symptom, did not recognize. It might be truly said that the psychiatrist's practice with older children is built on the pediatrician's dictum that the child will grow out of his difficulties as he grows older. It would be good education for the pediatrician to look ten years later at those 5 year old children whom he thought would grow out of their difficulties. I am not suggesting that some children do not grow out of their difficulties, but the pediatrician cannot take it for granted that they will. He must have some training which will enable him to evaluate young children's problems and prognosticate on the basis of his findings whether they will or will not disappear. There is nothing in the older pediatrician's training which gives him that prognostic skill when handling behavior difficulties.

In conclusion, I should like to point out that the pediatrician's patients themselves are making physicians mental hygiene-conscious. I know of many cases in which parents have insisted that their pediatrician recommend a psychiatrist for a child who is being unsuccessfully treated for behavior problems by their family physician. I believe that this trend will develop unless the pediatrician recognizes that ignorance cannot be the basis of self-assurance.

DR. LAWSON G. LOWREY: I have had a most unusual experience tonight. In the first place, I have heard a pediatrician castigate Dr. Wile for reading the only intelligible paper I ever heard him read. In the second place, I have heard a pediatrician use what he called psychiatric language, which I could not even understand. The question comes up, What has happened? Are pediatricians at last beginning to discover that there are some points of actual honest observation that they can make about the elementary facts of human behavior and human relationships as exemplified in the behavior of children, and, more important than that, that they can express them in language that one can understand without having to resort to those peculiar formulas which are very satisfying to one who finds them satisfying and are very troublesome to one who does not? Are they coming to a common ground of actual working relationships on the basis not only of common vocabulary but, much more important, of common sense?

I am appreciative of the series of pictures shown. They were delightful. We have been collecting pictures like that from the papers for years. Those that were shown represent direct observations, slightly or very much dramatized, of what is actually happening. To most persons they are simply "a laugh." But when, as was done tonight, some of the implications therein stated about the future behavior of these persons and some of the extremes in the problem of human relationships are pointed out, there is something well worth careful study. It is much more important than trying to learn what "psychopathic personality" or some of the other phrases which are now common in pediatric literature mean, because it is of the essence of which life is made.

Nothing would give me greater personal pleasure than to see a closer relationship between the group of pediatricians and the psychiatrists who are interested in children of all ages and what is happening to them. But if the pediatrician thinks that all the problems that he sees are going to "clear up" without a greater psychologic understanding and without a greater digging into the problems of both the child and the parents, there are breakers ahead. This is exactly what physicians have been doing from time immemorial. What does a physician do when he has a neurotic patient in whom he cannot find any physical disorder? He examines him and then pats him on the back and says that there is nothing the matter with him. What does the neurotic do? He worries twice as much. He asks himself why he has all these symptoms. Maybe he has a mental disorder. So that is not the most hopeful contribution to be made for the neurotic.

Finally, a great deal of the present difficult situation that physicians are in is dependent on what has been the absolute inadequacy of medical training with reference to the patient as a whole, including the fact that he has a mind and that part of that mind is emotion. We have been so interested in science that we have lost the patient. I have been teaching for twenty-five years, and I know something of what has been going on, even in hospitals; I can show examples in the hospital wards tomorrow, if any one doubts my word. We have come to forget the patient, and, worse still, we have forgotten that there are simple things in life and simple approaches to problems which frequently work when a complex approach will not. One of the most difficult things I have had to do in the past ten years in training postgraduate students is to get them to use the simple point of departure as an approach to the complex, instead of taking the complex as the point of departure from the simple.

DR. IRA S. WILE: I really ought not to say anything, because I am not sure that I shall be "intelligible." At the same time, I shall take the risk. I am interested in the comments of the first speaker, for while there were three speakers, his only comment was directed toward me. If my paper affected others as it did Dr. Johnson, who said that he did not know what I was talking about, it shows how necessary such talks are in a group of pediatricians.

I have been a pediatrician for many years, and I have had a clinic for behavior problems of children at Mount Sinai Hospital for sixteen years. More than twenty years ago I was talking in the same strain in which I was talking tonight, but apparently I was not understood then, and maybe I shall not be understood twenty years hence. However, the pediatrician will understand before that time has passed, because with the diminishing birth rate and a smaller number of children per family there will be a decrease in the problems of nutrition and fatigue, except that they will apply to the pediatrician himself. There will be, however, many more problems of behavior that the pediatrician will have to understand.

The psychiatrist is not on trial; I differ with my friend Dr. Levy on that point. It is the pediatrician who is on trial. Is he going to be abreast of the age in which he lives or not? Is he going to evidence awareness of the fact that pediatric science is moving or not? Unfortunately, the history of medicine is filled with ample evidence that when opportunity knocks at the door the physician and the pediatrician are not at home. They objected to the registration of persons with tuberculosis and resented all popular advances toward the control of syphilis. They have stood in the way of most hygienic and social advances which have been suggested but which have not emanated from themselves. Let us be honest about the situation. I am not here for the purpose of altercation. I am not even on the defensive, but on the offensive in the interest of pediatrics—perhaps too much so. If the pediatricians cannot understand my plea or statements they are in a bad way. I have used no word that is not in a pediatric textbook or in the pediatric nomenclature. Yet I am told that I am unintelligible. That is rather interesting. I happen to be a teacher, as is my good friend Dr. Lowrey—both of us have been teachers for a number of years. I have been teaching teachers, and I am at

present teaching in four colleges in New York. I could read this paper to my groups of teachers and have ample discussion, and not one of those laymen would say that I was unintelligible.

Who is going to bring about a change? It is not a question of fussiness. I think the three "F's" proper for Dr. Wilcox to emphasize. Dr. Wilcox and Dr. Lowrey have indicated what the current trend of thinking is. One makes cartoons of and burlesques, not things with which persons are unfamiliar, but things which belong to every-day life. The cartoon about broccoli and spinach has a meaning only in a land where spinach is forced on the young. If one tried to tell that story in France, no one would understand it. In Italy, perhaps, they would know what broccoli was. Why not recognize the facts of daily import? The newspapers of today are filled with comments about child study, child delinquency and mental hygiene in relation to the child. Where is the accent? It is primarily on childhood and on those who are most concerned with the care of the young. Yet pediatricians suggest they will have none of it. I say that they will have some of it, because a more educated public is coming to them with questions, asking what all this means: "What do they mean by intelligence tests?" "What does it mean when my child starts a bonfire in the schoolroom?" And so on. Is the pediatrician going to say, "I don't know. I have my doubts?" His status does not permit it. His responsibilities do not permit it. Therefore, I say that my paper may be unintelligible, but I think that I am understood.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Jan. 15, 1935

STANLEY GIBSON, M.D., *President, Presiding*

SOME OF THE MORE IMPORTANT AND PRACTICAL ASPECTS OF ENDOCRINOLOGY. DR. ANDREW C. IVY (by invitation).

The endocrine glands reviewed were the parathyroids, the thymus and the anterior lobe of the hypophysis.

The effects of chronic parathyroid deficiency on the teeth, bones and lens and on hearing were discussed. It was pointed out that the parathyroids are directly related to calcium and phosphorus metabolism, particularly in regard to the mobilization and regulation of the calcium and phosphorus balance between the blood and tissues. Parathyroid extract stimulates the osteoclasts to liberate calcium. Under its influence calcium may be removed from the bony depots and deposited in a callus. Vitamin D deficiency and parathyroid deficiency are analogous in a number of respects, but there are striking differences. Vitamin D does not act via the parathyroids, since this vitamin when administered cures rickets and causes hypercalcemia in the absence of the parathyroids. The relation of the parathyroids to osteomalacia, osteitis fibrosa cystica and other diseases of the bony skeleton was discussed.

The relation of the thymus, thyroid and ovaries to calcium metabolism was briefly considered, and the importance of the following factors in calcification, bone formation and growth was mentioned: the blood calcium content and form, the blood phosphorus content, the p_H of the plasma, the thyroid and parathyroid, the intake of calcium and phosphorus in food, the effective alkalinity or acidity of food, the reaction of the intestinal contents, the absorption of fats, bile, the vitamin D content of food and of the body, the excretion of calcium and phosphorus by the intestine and kidneys, and the anterior lobe of the hypophysis.

The effects of hypophysectomy and a hypothalamic lesion were compared, the observations of P. E. Smith on the rat being used for this purpose. The pro-

duction of two specific hormones by the anterior lobe of the hypophysis has been established beyond doubt; these are (1) the growth hormone, or somatotropin, and (2) the gonad-stimulating hormone, or gonadotropin. The evidence that three other specific hormones, namely, (3) the lactogenic hormone (an anterior pituitary hormone), (4) the thyrotropic hormone and (5) the adrenotropic hormone, are also produced is impressive. There is also strongly presumptive, if not crucial, evidence that the gonadotropic hormone is of two types, one of which stimulates the follicles of the ovaries to ripen (the follicles-stimulating hormone), while the other stimulates the luteal cells (luteinizing hormone). The other alleged effects of anterior lobe extracts, which require further study, are: (1) pancreatropic action, (2) diabetogenic action, (3) acetonemia-producing action, (4) action on the relation between the intake and output of water and (5) uterine bleeding effect.

The following diseases were discussed as being related to the anterior lobe: giantism, acromegaly, pubertas praecox, pituitary infantilism, pituitary eunuchoidism, pituitary myxedema, Simmonds' disease, Fröhlich's syndrome, Cushing's disease, Schüller-Christian disease and Laurence-Biedl disease. The latter two diseases are related only remotely, if at all, to disorder of the anterior lobe.

DISCUSSION

DR. C. A. ALDRICH: I have been much impressed by Dr. Ivy's masterful summary of this subject.

I wish to report briefly a case of Simmonds' disease that I saw in the past year, in a girl, aged 14. The basal metabolic rate was —34; the patient had lost 35 pounds (15.9 Kg.) in the course of a year and looked like a patient with cancer of long standing. Menstruation, which had been present for a year, had ceased. She showed marked microsplanchnia and a small liver, heart and stomach. We tried thyroid therapy to begin with, with no success; the basal metabolic rate fell instead of rising. Then we tried an anterior lobe pituitary preparation with thyroid extract, with no result; but when we gave large doses (2 cc. daily) of anterior lobe pituitary preparation alone she gained 1½ pounds (0.75 Kg.) a day for several days. Since then she has gained less rapidly, but is doing fairly well. She has not menstruated again, although we are giving pituitary sex hormones as well as anterior lobe pituitary preparation. This child is the youngest patient with this condition of any whose cases I have seen reported.

DR. ARTHUR H. PARMELEE: Two points in regard to this subject appealed to me particularly because of my individual interests. It has been stated by some that the hypophysis may be considered the governor of the endocrine system. Undoubtedly, from what Dr. Ivy said, the endocrine system has a close relationship with the vegetative nervous system. The close relationship between the hypophysis and the hypothalamus and, in turn, the close interrelationship of the hypophysis with the vegetative nervous system, seem interesting. As all the members know, I have been interested for many years in the new-born and have spoken of the reaction that is known as the engorgement of the breast, which occurs in practically all new-born infants born at full term, but which is almost universally absent, so far as I know, in premature infants. It is my belief that the absence of engorgement of the breast in the premature infant is probably due not to the absence of the hormone circulating in the new-born infant's blood, but more likely to immaturity of the vegetative nervous system and inability to make use of this hormone.

The other condition in which I have been interested is fat metabolism and the distribution of fat in lipodystrophy. This peculiar syndrome has never been explained, but in the majority of the cases reported the condition is associated with infection of the upper respiratory tract, infection of the tonsils or an acute contagious disease, such as measles, scarlet fever or diphtheria. In the cases reported this relationship seemed to be striking. The fact that one finds marked disturbances in metabolism following encephalitis, a disease which seems to have its origin in the upper respiratory tract and which often results in obesity or other

changes in the fat metabolism, and that an association exists between lipodystrophy and infection of the upper respiratory tract which might produce changes in the hypothalamic portion of the midbrain and disturbances of the vegetative nervous system, seems worthy of consideration. These conditions may prove to be closely related.

Dr. Ivy's discussion centered around the hypophysis more than any other gland and, I think, rightly so, because of the close relationship of this gland to the central nervous system and to all the other endocrine glands.

DR. A. LEVINSON: I was greatly impressed with Dr. Ivy's discussion. I am glad that he spoke of pitressin as having sometimes an antidiuretic effect and at other times a diuretic effect. Recently, my associate and I, in working on meningitis, used pitressin in order to decrease the urinary output; we found that this was not decreased.

I was rather surprised that Dr. Ivy, in speaking of cases of so-called status lymphaticus, said that death in these cases is due to marked enlargement of the thymus, resulting in obstruction of the trachea and larynx. This does not seem plausible. In acute infections of any kind the thymus is enlarged, yet does not cause death. I have the impression that status thymicolymphaticus, if it exists, is due not to the size of the thymus but to some other mechanism.

I should like to ask Dr. Ivy's opinion about using growth hormone in cases of chondrodystrophy. I have put this question to many physiologists and endocrinologists in this country. I have seen a case of this type in a child whose parents are eager that something be done.

DR. JOSEPH BRENNEMANN: Dr. Ivy mentioned a condition that is generally called Fröhlich's syndrome. If I remember correctly, Fröhlich described this as due to a tumor of the hypophysis which involves the sella turcica. What is the usual sign that one associates with Fröhlich's syndrome? Can any definite anatomic lesion be found?

I wish to express my surprise at Dr. Ivy's statement in regard to status thymicolymphaticus. I think that few physicians, from clinical and pathologic experience, believe that the sudden death in these cases is due to pressure. I have always thought that there was a certain definite condition in association with thymic enlargement that one might speak of as hyperplasia, in which the thymus may be large, and yet this is not associated with status thymicolymphaticus, if by that one means the acute condition that is often assumed to be the cause of sudden death.

DR. ANDREW C. IVY: I am grateful to the speakers for discussing my lecture.

In regard to Fröhlich's syndrome, it is difficult to say, from what is now known of the hypophysis and the thalamus, whether the condition is due to disturbance of the former or of the latter. I suspect that most of the cases are mixed—that is, some of the symptoms are due to disorder of the anterior lobe of the hypophysis and others are due to the hypothalamic disturbance. Of course, Fröhlich's syndrome is relatively rare, which is fortunate.

In regard to the lipodystrophies, I have been interested in them from the theoretical point of view for years. I became especially interested in the problem when Dr. Rony and I were studying the deposition and mobilization of fat. I believe that the hypothalamus is concerned, but there is no direct proof. I cannot believe that lipodystrophy is due to a hormonal disturbance. Hormones do not pick out one side of the body (hemilipodystrophy) unless there is definite peripheral or somatic disturbance. The condition is more likely due to some nervous disturbance, and if hormones are concerned, they play only an indirect rôle.

In connection with status thymicolymphaticus, I should have referred to the following incident: At an autopsy which I attended the clinical diagnosis was status thymicolymphaticus, but the pathologist thought that a more accurate diagnosis would have been *causa mortis incognita*. Apparently I did not make my views concerning status thymicolymphaticus entirely clear. On an endocrinologic

basis, I do not believe that such an entity as status thymicolymphaticus exists; but if an enlarged thymus is concerned in the cause of sudden death it operates only to exaggerate more fundamental causes of dyspnea, cough and cyanosis, such as infection of the respiratory tract.

In regard to pitressin, it is known that when pituitary extract is administered under certain conditions it has a diuretic action and when administered under other conditions, an antidiuretic action. In diabetes insipidus it is an antidiuretic. I gave an example showing how one can reverse the action of pitressin by the mode of administration. Why that happens no one knows. I suspect that it may be due to a factor relating to the dosage.

In regard to the treatment of Dr. Levinson's patient, I know of nothing to suggest. I am not a therapeutic nihilist, and I do not encourage haphazard organotherapy; but I believe in using the known active preparations that are available so far as one knows that they will not harm the patient and so far as they are physiologically rational. Clinically, one must be exceedingly careful in interpreting results when they are obtained. The clinical use of most of the hormone preparations of the anterior lobe of the hypophysis and of the gonads, which are active in animals under controlled conditions, is still in the experimental stage. Many years of careful study will be required before one will be able to state correctly the clinical indications for and the effectiveness of the hormones of the anterior lobe which I discussed this evening.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

Twelfth Annual Meeting, Brockville, Canada, June 1 and 2, 1934

H. P. WRIGHT, M.D., *President*

R. R. STRUTHERS, M.D., *Secretary*

(*Concluded from p. 824*)

Third Session

Saturday, June 2, 2 p. m.

HEREDITARY DEFORMING CHONDRODYSPLASIA. DR. A. E. CHILDE (by invitation), Montreal, and DR. H. B. CUSHING, Montreal.

Hereditary deforming chondrodysplasia (multiple exostoses) is congenital. Among a series of 6 cases discussed in this paper there was a definite familial history in 3. This disease is a well marked clinical entity, but the degree of involvement varies tremendously, from the minor cases in which the disease may be difficult to diagnose to the extremely marked cases in which a diagnosis may be made at a glance. In the less marked cases examination of the hands and feet is often of considerable value in the differential diagnosis. Deformities of the hands and of the feet occur constantly, often with few other noticeable changes. Sir Arthur Keith's explanation of the deformities that are found is probably correct. He suggests that the modeling process which occurs during growth and which prunes and reforms the new bone in the region of the cartilaginous growth disk at the end of the shaft is profoundly retarded or completely arrested. Consequently growth of bone occurs, but it is lawless. Only the parts of the skeleton that are derived from cartilage are affected. It is believed that hereditary deform-

ing chondrodysplasia is probably considerably more general than has formerly been supposed, and that many of the minor cases are usually unrecognized.

DISCUSSION

DR. DONALD PATERSON, London, England: The roentgenograms shown were excellent examples of this disease. Dr. Fraser has seen many cases at meetings of the Royal Society of Medicine and has always maintained that this disease was familial and hereditary, and that one could trace it from one generation to another. If one will consult the new textbook by Carson and Berlinger one will find some excellent views which the authors claim are associated with this disease. The book contains good roentgenograms. In cases in which the blood was tested it was found to be normal. In the cases that we have seen so far the thumb and great toe were little affected. Often there is a greater effect there in the most marked cases. In the less marked ones these parts are usually separate, and the remaining toes and fingers seem to be more affected.

ASSOCIATION OF A DIET LOW IN MINERALS WITH DECREASED GROWTH, RESISTANCE AND INTESTINAL MOTILITY. DR. ELIZABETH CHANT ROBERTSON (by invitation), Toronto, and DR. F. F. TISDALL, Toronto.

When white rats were fed, from weaning, diets very low in minerals, their increase in weight in the first twenty-four days was about half that of adequately fed controls. The resistance of these mineral-deficient rats, as measured by the percentage of survivors after oral infection with a rat typhoid bacillus, was also much lower than that of the controls.

After the feeding of 6 mg. of carmine, the mineral-deficient rats excreted this substance for from ten to seventeen days, whereas in the adequately fed controls carmine was not found after four or five days. The presence of carmine was established by examining drops of a suspension of the feces microscopically. The carmine could not be seen with the naked eye for such long periods, but the mineral-deficient animals showed gross carmine for a much longer time (from six to seven days) than the normal controls (from three to four days). In other words, a considerable degree of intestinal stasis was present in the animals fed the diet low in minerals. The presence of the stasis was confirmed by experiments in which a series of rats on the two diets were fed carmine and then one of each group was killed and the intestinal tract examined for carmine each day. The intestines of the mineral-deficient animals contained considerably more material than those of the normal controls, which would suggest that the stasis was due to atony. The stasis of the mineral-deficient rats could be cleared up by feeding the rats an adequate diet for four weeks. Feeding an adequate diet for one week only almost cleared up the stasis. Added vitamin B did not increase the speed of excretion of the carmine.

The addition of as much calcium to the mineral-deficient diet as was present in the adequate diet did not relieve the stasis to any appreciable extent. However, when both calcium and potassium were added the intestinal atony was relieved, which would suggest that the potassium had a stimulating effect on the intestinal motility. Confirmatory experiments are in progress.

From Sherman's tables it was found that the foods that were richest in potassium were usually laxative, for example, prunes, spinach, bran, flaxseed, figs and beans. The child's need for potassium is high, and this element is unfortunately very soluble and is commonly discarded in the water in which vegetables have been cooked.

RELATIVE ABSORPTION OF ORGANIC AND IORGANIC PHOSPHORUS. DR. C. B. WELD (by invitation), Toronto, and DR. T. G. H. DRAKE, Toronto.

The phosphorus balance of 4 mature dogs which were on an adequate diet low in phosphorus was determined. Organic phosphorus in the form of sodium glycero-

phosphate or inorganic phosphate in the form of dibasic sodium orthophosphate was added to the diet of the dogs during definite periods. The amount added corresponded in most cases to 500 mg. of phosphorus daily, and all the periods of administration were of two weeks' duration.

No difference in the absorption of phosphorus in these forms was observed, nor was any difference noted in the amount retained by the animal.

The presence of phosphatase in the intestinal lumen of infants (autopsy material) was demonstrated.

KLIPPEL-FEIL SYNDROME OR WEBBED NECK. DR. H. S. MITCHELL (by invitation), Montreal, and DR. H. B. CUSHING, Montreal.

Reference is made to the original description of this condition by Klippel and Feil, who emphasized three main features: shortening or absence of the neck, a low hair-line and limitation of the movements of the head and neck. Comparatively few cases have been reported, but as several authors have reported several cases each, it is likely that the condition is more common than has been supposed. Reference is made to the unknown etiology and the clinical appearance, as well as to the roentgen findings. In the diagnosis congenital torticollis, tuberculosis and syphilis must be considered. Treatment is palliative. The prognosis is very good so far as expectation of life is concerned.

Six cases are reported, in 2 of which the patients came to autopsy in infancy. Detailed descriptions of the anatomic specimens are given, with special reference to the spinal nerves. In each case the normal number of intravertebral foramina were present, although the vertebral bodies could not be identified.

DISCUSSION

DR. G. F. BOYER, Toronto: What is your impression of the mental activity of children with this condition? I have under observation one patient who is very bright. She is at the top of her class in school, but she seems mentally unstable.

DR. DONALD PATERSON, London, England: I have seen several of these patients. The condition varies enormously in severity. I did a postmortem examination some years ago at Great Ormond Street Hospital. When the actual cord came into view, the whole of the posterior part of the arch of the vertebrae was absent.

DR. ALAN BROWN, Toronto: I was extremely interested in seeing the pictures and hearing the anatomic description of the condition. I have seen only 2 cases. Both the patients were small and short; their mentality was within normal range, and there was no congenital deficiency that I know of.

DR. H. S. MITCHELL, Montreal: In regard to the mental condition, so far as I know, there is only one case in the literature in which there was definite mental involvement. The patient whose case I have reported was a deaf-mute and probably mentally affected. No neurologic condition was apparent, except an involuntary movement in one extremity; it may not be correct to attribute that to this condition.

EFFECT OF A SPECIAL CEREAL VITAMIN B ON THE RATE OF GROWTH OF NORMAL CHILDREN. DR. JOHN R. ROSS (by invitation), Toronto, and DR. PEARL SUMMERFELDT, Toronto.

The clinical effects of vitamin B deficiency are now fairly well known. Anorexia, decreased intestinal motility and tone, diminished gain in weight and decreased resistance to infection are the chief effects.

Morgan and Barry showed that feeding wheat germs to undernourished children produced a striking gain in weight.

Bloksom fed vitamin B in the form of dried brewers' yeast to infants and children under 2 years of age and found that they gained at a considerably greater rate than control infants and children on ordinary feedings.

During the winter of 1931 a group of children were fed Mead's Cereal, which has been shown to contain fairly large amounts of vitamin B and iron. A control group were fed similar amounts of ordinary cereals.

During the last eight months an extensive nutritional study has been made with a larger group of children who were in an orphanage situated in the country, in which the living conditions were very satisfactory with regard to periods of rest, recreation and exercise and other features.

The ages of the children were from 5 to 14 years, and they had been in the institution for at least three months before the period of observation began, so that they had become accustomed to the institutional regimen. Their diet was found to be a very good one.

At the beginning of the investigation these children were to all intents and purposes normal, receiving a well balanced diet and living in a good environment. Their weights at the beginning of the experiment did not deviate by more than 10 per cent from the normal weight and height for their ages, as given in the tables of the Toronto Health Department.

They were divided into three groups of approximately 25 children each, and each group had about equal numbers of girls and boys of similar ages. One group was kept on the ordinary diet to which they had been accustomed. These children received 3 ounces (85 Gm.) of oatmeal or farina for breakfast each morning. The second group received exactly the same diet, except that 3 ounces of Pablum, which is a precooked form of Mead's Cereal, replaced the ordinary cereal for breakfast. The third group were fed the same diet as the control group, with the addition of 6 Gm. of a vitamin B concentrate made from wheat germ and brewers' yeast. This concentrate supplied more than twice the amount of vitamin B that was contained in the 3 ounces of the precooked meal.

The children were weighed twice a month for six months. In the following slide are the average weights during this time. It is seen that the group fed the special cereal gained more than twice as much as the control group. The group fed the vitamin B concentrate also gained more than the control group, but not as much as the group fed the special cereal. From these results it would appear that the growth-promoting effect of vitamin B is only partly responsible for the striking gain in weight of this group. We are not prepared to offer a definite explanation as to what this additional gain is due, except that it may be partly caused by the increased consumption of calcium, phosphorus, iron and copper.

During the course of this investigation we also made monthly determinations of the hemoglobin on all the children by the Newcomer method. Since the special cereal contains from 17 to 24 mg. of iron per ounce (28.3 Gm.), as compared with 4.5 mg. for oatmeal, it is not surprising that the group fed the special cereal showed a considerable rise in hemoglobin over the control group at the end of the six months' period.

DISCUSSION

Dr. H. P. Wright, Montreal: These findings are, of course, interesting from a scientific point of view, but is it, from a clinical point of view, of any advantage to make these children gain more weight? Sometimes I think that weight is overemphasized.

Dr. Alan Brown, Toronto: One does not know what the normal weight is. One tries to strike an average.

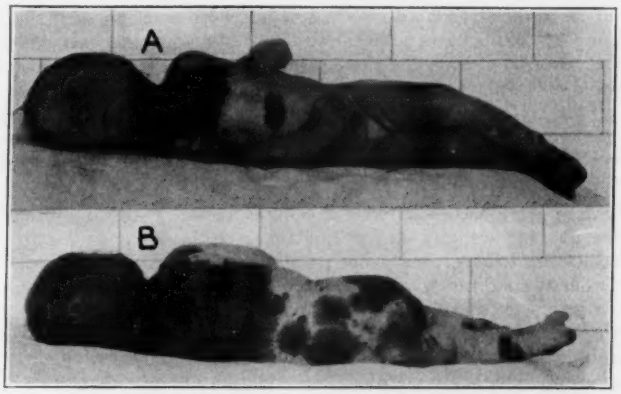
Naevus Pigmentosus. Harold Palmer, Brantford.

This case is presented to the Society as being of probable interest, owing to the extensive area involved.

The term nevus is derived from the Latin word *naevus,* meaning a blemish or mark. Although the majority of these deformities are present at birth, many may not appear until after infancy or even after childhood. Several classifications

have been submitted by various observers, but nevi may be divided, in general, into two chief groups, according to their embryonic origin, as they develop from both the mesoderm and the ectoderm. Those developing from the former are known as the vascular nevi and are characterized by hyperplasia of the blood or lymph vessels. Those of the second or nonvascular group develop from the ectoderm, and are either soft or warty, with more or less pigmentation. Most of the latter type show characteristic groups of globular cells, with vacuoles and pigment granules, called nevus cells.

In the case which I shall report the patient presented both groups, although the nonvascular type predominated. The patient was a boy who had been born at full term at the Brantford General Hospital on Sept. 13, 1932; the weight at birth was 8 pounds and 11½ ounces (3,954.7 Gm.). The family history is not significant. Both parents are of British descent and blond. Physical examination showed a well developed, well nourished boy with lips, ears and nails slightly cyanosed. Anteriorly, scattered throughout the skin, were numerous dark brown and purplish-red areas, varying in size from a few millimeters to from 7 to 8 cm. in the greatest dimension. Over the right cheek and the entire upper part of



A, anterior, and *B*, posterior, view of patient.

the chest these areas were merged. Posteriorly, the discoloration was even more extensive, for beginning at the vertex of the head, involving both ears and the neck and extending down to the lumbar region no normal skin was evident, the surface appearing dark purplish red and brown. Over the head, ears and shoulders were many raised, rounded, warty excrescences, ranging up to 2 cm. in diameter, some of which felt rather soft and fluctuant. There was little hair present on the back of the head, although there was a profuse growth, black in color, on the crown and temples, extending down the left side of the head onto the cheek. There were also large pigmented areas on the lumbar and gluteal regions, with smaller ones on the legs. In the midline of the back, above the sacral region, was an irregular, pigmented swelling, about 5 by 7 cm. in size, devoid of hair.

Otherwise physical examination showed no abnormality, with the exception of a few moist râles, heard over the base of both lungs, posteriorly. The infant was somewhat listless, with a feeble cry, and nursed only fairly well. On the second day a large protuberance situated behind the right ear ruptured, and about 3 or 4 cc. of brownish fluid drained out, leaving an ulcerated surface. On the fourth day a pustule a few millimeters in diameter appeared on the medial surface of the right leg. The infant's color remained slightly cyanosed in spite of stimulants and other treatment; his cry was feeble, and he died on the fifth day.

Autopsy revealed a slight degree of pulmonary atelectasis and hemorrhagic nephritis. A culture from the pustule on the right leg showed the presence of Staphylococcus aureus.

A section through a flattened nevus showed the epidermis to be quite thin, covering wide hypertrophied papillae of the corium. In the latter, were dense masses of nevus cells, large groups of which contained many brownish-black pigment granules near the surface. The unpigmented cells extended throughout the entire thickness of the true skin and in places down into the subcutaneous fat.

A section through one of the raised papillomatous areas showed the picture just described, with the additional feature of extreme vascularity, giving the nevus an angiomatous appearance. Thin, long interpapillary processes extended down from the overlying skin. In places the epidermis had disappeared and the vessels near the surface had become thrombosed. The base of superficial ulcerations was made up of a thin layer of necrotic tissue.

THE PEDIATRICIAN AND THE PROBLEM PARENT. DR. A. P. HART, Toronto.

In this era of rapidly changing conditions the pediatrician and general practitioner are constantly meeting with behavior problems in children. Although such influences as those of the movies, radio, motor car and comic strip are pernicious, one feels that since the time of Cain and Abel there have always been problems in the bringing up of children and that there probably always will be. Recalling one's own childhood, it would seem that the children who gave the least trouble and turned out the most creditable were the ones whose parents maintained their authority with a reasonable but firm hand. It is believed that the present-day difficulties only emphasize the necessity for the exercise of a more vigilant attitude in retaining control by those to whom it rightfully belongs, i. e., the parents, if children are to escape the pitfalls from the added hazards to which they are subjected.

The psychologists have leapt into the van with their parent education movements, their lectures to school and home clubs and to the lay public in general on mental hygiene and other aspects of education. They are making advances and have offered helpful suggestions. Doubtless in many cases of intricate problems in behavior they are better able to arrive at a solution from their specialized training in these lines than is the pediatrician or the general practitioner. The author gravely doubts their wisdom in such promiscuous teachings on a subject so intricate and in such a state of flux. He recalls being intensely intrigued by the theory of Freud when a student twenty-three years ago. After attending a clinic on psychoanalysis twice weekly for six months conducted by one of its foremost exponents in the British Empire realization came that this beautiful theory was intricate and did not lend itself easily to application, even in the hands of one of its most able and intelligent devotees. He believes that even after all these years the same may be said of it, and that psychology also has not reached the stage where it may be readily grasped and definitely applied by the lay person. To a large number of parents it is merely confusing, so that they are bewildered as to what to do in even the simplest circumstances. In that state of mind they completely lose their authority. He believes that parents who maintain their authority with firmness and decision, even though sometimes they may be wrong, will succeed where others will fail miserably.

He believes that the pediatrician, because of his close contact with the mother and family, is the proper person to offer timely advice in many of these cases. He can also assure the mothers who are not blessed with unending patience and pliability that they have not committed the unpardonable sin when they have lost their patience with their child, and that they have probably done him or her a lot of good. Often assuring the mother that she is right in being perfectly firm and that she is not going to produce an inferiority complex or some other complex by so doing lifts a weight from her shoulders.

Dr. Robert Hutchison is quoted regarding parental hypochondriasis. He believes that it is sometimes unwittingly fomented by pediatricians and physicians, and that they might well refrain from giving parents the impression that the rearing of a healthy child is a task of superhuman difficulty.

As a last word, he believes that the pediatrician might well impress on parents the fact that the place to train a child is in the home; that if the home does not train him, the school has to train him; if the school does not train him, the world has to train him, and if the world does not train him, the jail has to train him, and each one is a harder master.

Book Reviews

Conception Period of Women. By Dr. K. Ogino. Price, $1. Pp. 93, with 22 charts. Harrisburg, Pa.: Medical Arts Publishing Co., 1934.

This small book deals with the probable conceptive period and its negative phase of two sterile periods, with a consideration of their use in the limitation of the number of pregnancies.

According to Dr. Ogino's theory (for which he states his evidence), the conceptive period is between the twelfth and nineteenth day before the next menses. The sterile periods are from the first to the ninth day, including the first day of the menses, and between the seventeenth and twenty-eighth day in a woman with menstrual periods of the twenty-eight day type. These dates are calculated for each person according to the previous menstrual calendar.

Dr. Ogino points out that some authorities may disagree with him as to the length of life of the sperm, the length of life of the ovum and the psychic influence on the menses-provoked ovulation. He attempts to meet these differences in his little exposition. Nevertheless, he holds that the theory has its practical application, especially among persons who because of religious convictions or other reasons prefer not to use artificial means for contraception.

The book is written for the popular reader. Such a person may find it too technical. It is, however, worth the physician's time, because it states briefly and concisely the modern conception of the relation of ovulation to menstruation, also the rôle of the pituitary gland in the menstrual cycle. The value of Ogino's theory for the prevention of conception can be established only after a great deal of practical application.

In an appendix to the book the publishers reproduce Miller, Schulz and Anderson's article "The Conceptive Period in Normal Adult Women," published in *Surgery, Gynecology and Obstetrics,* June 1933.

The Care and Feeding of Children. By L. Emmett Holt Jr. Fifteenth edition. Price, $1.25. Pp. 246. New York: D. Appleton-Century Company, Inc., 1934.

This book is dedicated to young mothers and is intended to inform them of the common facts about infants and children which they should know. It is written in question and answer form—the questions being those frequently asked by mothers and the answers those given by pediatricians. Emphasis is placed primarily on the care of the well child and only secondarily on the care of the child during illness.

The chief changes in this edition occur in the chapter on infant feeding, although there are other minor changes and additions to bring the material up to the latest available knowledge.

There are five chapters: "The Care of Infants," "Infant Feeding," "Premature Infants," "Older Children" and "Miscellaneous." Mental hygiene is little discussed. It would seem that more discussion of this subject would be appropriate for a book of this kind.

Synopsis of Pediatrics. By John Zahorsky, M.D., and T. S. Zahorsky, M.D. Price, $4.50. Pp. 350, with 77 illustrations and 6 colored plates. St. Louis: C. V. Mosby Company, 1934.

This small compact volume is intended for the use of students of medicine. As much as possible has been eliminated. Bare facts have been put down, and no attempt is made at giving references to the literature. The authors acknowledge reference to other textbooks in the preface. All redundancy has been removed, and the material has been boiled down to the smallest possible quantity. This will serve as a usable book for students. While the illustrations are numerous, most of them are not original, but are taken from other textbooks. If one remembers that this book is not to be used as a reference book, but is to be supplemented by a more extensive textbook on pediatrics, one will be able to recommend it to students in medical schools.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.
Place: Bâle, Switzerland: Time: September 1935.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.
Place: Newcastle, County Down, Ireland. Time: May 3-4, 1935.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. R. C. Jewesbury, 5, Wimpole St., London, W. 1.
Secretary: Dr. Helen Mackay, 28, John St., London, W. C. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4: 30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. A. Graeme Mitchell, Children's Hospital, Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Atlantic City, N. J. Time: June 10-14, 1935.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New York. Time: June 7-8, 1935.
Region I. Place: Philadelphia. Time: Oct. 11-12, 1935.
Regions II and III. Place: St. Louis. Time: Fall, 1935.
Region IV. Place: Seattle, with North Pacific Pediatric Society. Time: Aug. 9-10, 1935.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Borden S. Veeder, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Wade Park Manor, Cleveland. Time: May 2-4, 1935.

Canadian Society for the Study of Diseases of Children

President: Dr. D. P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Buffalo, N. Y. Time: June 1935.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Joseph Stokes Jr., Children's Hospital, Philadelphia.
Secretary: Dr. A. A. Weech, Babies Hospital, New York.
Place: Atlantic City, N. J. Time: May 1935.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Armin Rembe, Stimson Bldg., Seattle.
Secretary: Dr. Frank H. Douglass, 1227 Medical and Dental Bldg., Seattle.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Oliver W. Hill, 301 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Charles Abbott, 1817 Broad St., Tuscaloosa.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Benjamin Bashinski, 700 Spring St., Macon.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Lonis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Matthew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. John Signorelli, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Edwin A. Socola, 1027 Canal Bank Bldg., New Orleans.
Place: New Orleans. Time: April 29, 1935.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George Sincerbeaux, 6 William St., Auburn.
Secretary: Dr. John D. Craig, 12 E. 11th St., New York.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Place: Flint. Time: September 1935.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. N. C. Womack, Jackson Infirmary, Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. C. V. Rice, 222 Wall St., Muskogee.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Place: Oklahoma City. Time: May 1935.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Francis T. O'Donnell, 345 North Main St., Wilkes-Barre.
Secretary: Dr. Theodore O. Elterich, 119 S. Highland Ave., Pittsburgh.
Place: Harrisburg. Time: Sept. 30-Oct. 3, 1935.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Julian P. Price, Medical Bldg., Florence.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Arthur G. Jacobs, 1193 Madison Ave., Memphis.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.

TEXAS PEDIATRIC SOCIETY

President: Dr. Ramsay H. Moore, 3600 Fairmount St., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. P. McDowell, 142 W. York St., Norfolk.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Harry M. Greenwald, 499 Ocean Ave., Brooklyn.
Secretary: Dr. Sylvan D. Lazarus, 847 Lincoln Place, Brooklyn.
Place: Medical Society of County of Kings Bldg., 1313 Bedford Ave., Brooklyn.
Time: Third Wednesday of each month from October to May, 8:30 p. m.

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. C. V. Mulligan, 17 Walmer Rd., N., Toronto.
Secretary: Dr. T. B. Verner, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Stanley Gibson, 9503 Prospect Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: John B. Murphy Memorial Bldg. Time: Third Tuesday of each month

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Earl W. May, 1551 Woodward Ave., Detroit.
Secretary: Dr. E. A. Wishropp, 10 Peterboro Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Frank Lancaster, Medical Arts Bldg., Houston, Texas.
Secretary-Treasurer: Dr. A. A. Little Jr., 817 Holman Ave., Houston, Texas.
Place: Houston Club: Time: Third Monday of each month.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y.: Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwuakee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Harry Bakwin, 132 E. 71st St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. O. W. Rowe, 205 W. 2nd St., Duluth, Minn.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Place: Minneapolis. Time: Spring, 1935.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Carl K. Wagener, Jenkins Arcade, Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 616 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklln St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: Nov. 22-23, 1935.

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